```
=> d his

     (FILE 'HCAPLUS' ENTERED AT 12:38:30 ON 06 FEB 2003)
                DEL HIS Y
                E VIRUS/CT
                E VIRUS+OLD/CT
L1         247509 S VIRUS## OR SINDBISVIR? OR ALPHAVIRUS?
L2           1543 S SINDBIS?/AB
L3           1393 S L1 AND L2
L4            118 S ALPHA VIRUS? OR (ALPHA VIRUS?)/AB
L5           1483 S L4 OR L3
L6         162214 S (VIRUS OR VIRUSES)/CT
L7            567 S (SIGNAL (3A) TRAP?)/AB OR SIGNAL (L) TRAP?
L8              1 S L7 AND L5
L9              9 S L7 AND L1
L10             9 S L8 OR L9
L11         77894 S (MEMBRANE# OR SECRET?) (L) PROTEIN#
L12            53 S L11 AND L7
L13             1 S L12 AND L1
L14             2 S L12 AND ?VIRUS?/AB
L15            10 S L10 OR L13 OR L14
                SET SFIELD BI
L16             1 S EXPORT? (S) GENETIC (3A) MATERIAL?
L17          8945 S (SIGNAL PEPTIDE#)/AB
                SET SFIELD OBI
L18          6521 S SIGNAL (L) PEPTIDE#
L19         13416 S L18 OR L17
L20           981 S L19 AND L1
L21        659908 S NUCLEIC ACID OR NUCLEOTIDE# OR DNA OR DEOXYRIBONUCLEIC OR OLI
L22           510 S L20 AND L21
L23           316 S L22 AND L18
L24         23028 S (CHIMER? OR FUSION ) (L) PROTEIN#
L25           116 S L24 AND L23
L26          1534 S CERULERIN OR OKADAIC ACID
L27             0 S L26 AND L25

     FILE 'REGISTRY' ENTERED AT 13:36:54 ON 06 FEB 2003
                E CERULERIN/CN
                E CERULENIN/CN
L28             6 S E3-8
                E OKADAIC ACID/CN
L29             1 S E3

     FILE 'HCAPLUS' ENTERED AT 13:37:36 ON 06 FEB 2003
L30          1740 S L28 OR L29
L31             1 S L30 AND L23
L32            16 S PROTEASE? AND L23
L33             8 S L32 AND L24
L34         17751 S LIBRAR?
L35            19 S L34 AND L25
L36             9 S L35 AND CDNA
L37             0 S EB VSS OR (EB VSS)/AB
L38            68 S FETTER OR FETTER/AB
L39             1 S L38 AND L23
L40         10337 S TRANSFECT?
L41             7 S L25 AND L40
L42            33 S L15 OR L31 OR L33 OR L36 OR L39 OR L41
```

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 13:45:46 ON 06 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    4 FEB 2003  HIGHEST RN 485752-98-5
DICTIONARY FILE UPDATES:   4 FEB 2003  HIGHEST RN 485752-98-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d que l28;d l28 cn rn 1-6
L28            6 SEA FILE=REGISTRY ABB=ON  PLU=ON  (CERULENIN/CN OR "CERULENIN
                 16"/CN OR "CERULENIN 18"/CN OR "CERULENIN, DIHYDRO-"/CN OR
                 "CERULENIN, HEXAHYDRO-"/CN OR "CERULENIN, TETRAHYDRO-"/CN)
```

↳ I could not find anything for cerulerin. Could it be ?cerulenin? (See claim 7)

```
L28  ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2003 ACS
CN   Oxiranecarboxamide, 3-[(4E,7E)-1-oxo-4,7-pentadecadienyl]-, (2R,3S)- (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Oxiranecarboxamide, 3-(1-oxo-4,7-pentadecadienyl)-, [2R-
     [2.alpha.,3.alpha.(4E,7E)]]-
OTHER NAMES:
CN   Cerulenin 18
RN   147000-16-6  REGISTRY

L28  ANSWER 2 OF 6  REGISTRY  COPYRIGHT 2003 ACS
CN   Oxiranecarboxamide, 3-[(4E,7E)-1-oxo-4,7-tridecadienyl]-, (2R,3S)- (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Oxiranecarboxamide, 3-(1-oxo-4,7-tridecadienyl)-, [2R-
     [2.alpha.,3.alpha.(4E,7E)]]-
OTHER NAMES:
CN   Cerulenin 16
RN   147000-15-5  REGISTRY

L28  ANSWER 3 OF 6  REGISTRY  COPYRIGHT 2003 ACS
CN   7,10-Dodecadienamide, 2-hydroxy-4-oxo-, (7E,10E)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   7,10-Dodecadienamide, 2-hydroxy-4-oxo-, (E,E)- (8CI)
OTHER NAMES:
CN   Cerulenin, dihydro-
CN   Dihydrocerulenin
```

RN 17397-92-1 REGISTRY

L28 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2003 ACS
CN Dodecanamide, 2-hydroxy-4-oxo-, (+)- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Cerulenin, hexahydro-**
CN Hexahydrocerulenin
RN 17397-91-0 REGISTRY

L28 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2003 ACS
CN Oxiranecarboxamide, 3-(1-oxononyl)-, (2R,3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dodecanamide, 2,3-epoxy-4-oxo- (8CI)
CN Oxiranecarboxamide, 3-(1-oxononyl)-, (2R-cis)-
OTHER NAMES:
CN (+)-Tetrahydrocerulenin
CN 2R,3S-Tetrahydrocerulenin
CN **Cerulenin, tetrahydro-**
CN Tetrahydrocerulenin
RN 17397-90-9 REGISTRY

L28 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2003 ACS
CN Oxiranecarboxamide, 3-[(4E,7E)-1-oxo-4,7-nonadienyl]-, (2R,3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7,10-Dodecadienamide, 2,3-epoxy-4-oxo- (8CI)
CN Oxiranecarboxamide, 3-(1-oxo-4,7-nonadienyl)-, [2R-[2.alpha.,3.alpha.(4E,7E)]]-
OTHER NAMES:
CN (+)-Cerulenin
CN **Cerulenin**
CN Helicocerin
RN 17397-89-6 REGISTRY

=> d que l29;d l29 rn cn
L29 1 SEA FILE=REGISTRY ABB=ON PLU=ON "OKADAIC ACID"/CN

L29 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 78111-17-8 REGISTRY
CN 1,7-Dioxaspiro[5.5]undec-10-ene-2-propanoic acid, .alpha.,5-dihydroxy-.alpha.,10-dimethyl-8-[(1R,2E)-1-methyl-3-[(2R,4'aR,5R,6'S,8'R,8'aS)-octahydro-8'-hydroxy-6'-[(1S,3S)-1-hydroxy-3-[(2S,3R,6S)-3-methyl-1,7-dioxaspiro[5.5]undec-2-yl]butyl]-7'-methylenespiro[furan-2(3H),2'(3'H)-pyrano[3,2-b]pyran]-5-yl]-2-propenyl]-, (.alpha.R,2S,5R,6R,8S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,7-Dioxaspiro[5.5]undecane, acanthifolicin deriv.
CN Acanthifolicin, 9,10-deepithio-9,10-didehydro-
CN Spiro[furan-2(3H),2'(3'H)-pyrano[3,2-b]pyran], acanthifolicin deriv.
OTHER NAMES:
CN 1,7-Dioxaspiro[5.5]undec-10-ene-2-propanoic acid, .alpha.,5-dihydroxy-.alpha.,10-dimethyl-8-[1-methyl-3-[octahydro-8'-hydroxy-6'-[1-hydroxy-3-(3-methyl-1,7-dioxaspiro[5.5]undec-2-yl)butyl]-7'-methylenespiro[furan-2(3H),2'(3'H)-pyrano[3,2-b]pyran]-5-yl]-2-propenyl]-, [2'R-[2'.alpha.[R*[1R*[2S*(R*),5R*,6R*,8S*],2E]],4'a.beta.,6'.beta.[1S*,3S*(2S*,3R*,6S*)],8'.alpha.,8'a.alpha.]]-

CN NSC 677083
CN **Okadaic acid**

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 13:46:09 ON 06 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his l1-127; d his l30-

(FILE 'HCAPLUS' ENTERED AT 12:38:30 ON 06 FEB 2003)
DEL HIS Y
E VIRUS/CT
E VIRUS+OLD/CT
L1 247509 S VIRUS## OR SINDBISVIR? OR ALPHAVIRUS?
L2 1543 S SINDBIS?/AB
L3 1393 S L1 AND L2
L4 118 S ALPHA VIRUS? OR (ALPHA VIRUS?)/AB
L5 1483 S L4 OR L3
L6 162214 S (VIRUS OR VIRUSES)/CT
L7 567 S (SIGNAL (3A) TRAP?)/AB OR SIGNAL (L) TRAP?
L8 1 S L7 AND L5
L9 9 S L7 AND L1
L10 9 S L8 OR L9
L11 77894 S (MEMBRANE# OR SECRET?) (L) PROTEIN#
L12 53 S L11 AND L7
L13 1 S L12 AND L1
L14 2 S L12 AND ?VIRUS?/AB
L15 10 S L10 OR L13 OR L14
SET SFIELD BI
L16 1 S EXPORT? (S) GENETIC (3A) MATERIAL?
L17 8945 S (SIGNAL PEPTIDE#)/AB
SET SFIELD OBI
L18 6521 S SIGNAL (L) PEPTIDE#
L19 13416 S L18 OR L17
L20 981 S L19 AND L1
L21 659908 S NUCLEIC ACID OR NUCLEOTIDE# OR DNA OR DEOXYRIBONUCLEIC OR OLI
L22 510 S L20 AND L21
L23 316 S L22 AND L18

```
L24        23028 S (CHIMER? OR FUSION ) (L) PROTEIN#
L25          116 S L24 AND L23
L26         1534 S CERULERIN OR OKADAIC ACID
L27            0 S L26 AND L25


     (FILE 'HCAPLUS' ENTERED AT 13:37:36 ON 06 FEB 2003)
L30         1740 S L28 OR L29
L31            1 S L30 AND L23
L32           16 S PROTEASE? AND L23
L33            8 S L32 AND L24
L34        17751 S LIBRAR?
L35           19 S L34 AND L25
L36            9 S L35 AND CDNA
L37            0 S EB VSS OR (EB VSS)/AB
L38           68 S FETTER OR FETTER/AB
L39            1 S L38 AND L23
L40        10337 S TRANSFECT?
L41            7 S L25 AND L40
L42           33 S L15 OR L31 OR L33 OR L36 OR L39 OR L41

     FILE 'REGISTRY' ENTERED AT 13:45:46 ON 06 FEB 2003

     FILE 'HCAPLUS' ENTERED AT 13:46:09 ON 06 FEB 2003

=> d .ca l42 1-133

L42  ANSWER 1 OF 33  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:22845  HCAPLUS
TITLE:                    Compositions and methods for inhibiting human
                          immunodeficiency virus infection by
                          down-regulating human cellular genes, and inhibitor
                          identification methods
INVENTOR(S):              Holzmayer, Tanya A.; Dunn, Stephen J.
PATENT ASSIGNEE(S):       Subsidiary No. 3, USA; Holzmayer, Andrew
SOURCE:                   PCT Int. Appl., 44 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND  DATE        APPLICATION NO.   DATE
     ------------------  ----  --------    ----------------  --------
     WO 2003002528       A2    20030109    WO 2002-US20964   20020701
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 2001-302157P  P  20010629
                                        US 2001-313252P  P  20010817
AB   The invention provides methods for identifying human cellular genes and
```

their encoded products for use as targets in the design of therapeutic agents for inhibiting or suppressing human immunodeficiency virus (HIV) infection. The invention also provides methods for identifying protective compds., including immunizing agents that inhibit HIV infection. The invention further provides compds. for use in the treatment or prevention of HIV.

IC ICM C07D

CC 1-5 (Pharmacology)
Section cross-reference(s): 3

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSR (**signal** sequence receptor), .beta. subunit, **TRAP** -.beta., target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT AIDS (disease)
Anti-AIDS agents
Antiviral agents
Apoptosis
Computer application
Computer program
Drug delivery systems
Drug screening
Drug targets
HeLa cell
Human
Human immunodeficiency **virus**
Macrophage
T cell (lymphocyte)
(compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT Human immunodeficiency **virus** 1
(tar binding protein, target; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT **Virus**
(viral stage assay; compns. and methods for inhibiting HIV infection by down-regulating human cellular genes, and inhibitor identification methods)

IT 484096-47-1 484096-48-2 484096-49-3 484096-50-6 484096-51-7 484096-52-8
RL: PRP (Properties)
(unclaimed sequence; compns. and methods for inhibiting human immunodeficiency **virus** infection by down-regulating human cellular genes, and inhibitor identification methods)

L42 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:6165 HCAPLUS

TITLE: Cancer cell cell-surface molecule and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods

INVENTOR(S): Poulsen, Hans Skovgaard; Pedersen, Nina; Mortensen, Shila; Sorensen, Susanne Berg; Petersen, Mikkel Wandahl; Elsner, Henrik Irgang

PATENT ASSIGNEE(S): Odin Medical A/S, Den.

SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000928	A2	20030103	WO 2002-IB3534	20020619

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2001-992 A 20010625
US 2001-301818P P 20010702

AB The invention describes methods for identification of mols. expressed at a different level on the cell surface of cancer cells compared to non-malignant cells and methods of identification of cancer-specific promoters to be used singly or in combination for delivery and expression of therapeutic genes for treatment of cancer. The invention furthermore describes targeting complexes targeted to cell surface mols. identified by the methods of the invention. In embodiments of the invention, the targeting complexes comprise the promoters identified by the methods of the invention. In addn. the invention describes methods of identifying binding partners for the cell surface mols. and the binding partners per se. Methods of treatment using the targeting complexes and uses of the targeting complexes for the prepn. of a medicament are also disclosed by the invention. Furthermore, the invention describes uses of the cell surface mols. or fragments thereof for prepn. of vaccines.

IC ICM C12Q001-68

CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 63

IT Bombesin receptors
Epidermal growth factor receptors
Insulin-like growth factor I receptors
Insulin-like growth factor II receptors
Insulin-like growth factor receptors
Nucleic acids
Promoter (genetic element)
RNA
Silencer (genetic element)
cDNA
mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study) (cancer cell cell-surface mol. and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods)

IT Simian **virus** 40
(large tumor antigen, nuclear targeting signal; cancer cell cell-surface mol. and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods)

IT Histones
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nucleic acid** binding agent; cancer cell cell-surface mol. and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods)

IT **Peptides**

7689-03-4, Camptothecin 18883-66-4, Streptozotocin 33419-42-0, Etoposide 52665-69-7, A23187 62996-74-1, Staurosporine 67526-95-8, Thapsigargin **78111-17-8**, Okadaic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer cell cell-surface mol. and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods)

IT 71-44-3, Spermine 124-20-9, Spermidine 25104-18-1, Poly-L-lysine 38000-06-5, Poly-L-lysine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nucleic acid** binding agent; cancer cell cell-surface mol. and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods)

IT 482671-30-7 482671-31-8 482671-32-9 482671-33-0 482671-34-1
482671-35-2 482671-36-3 482671-37-4 482671-38-5 482671-39-6
482671-40-9 482671-41-0 482671-42-1 482671-43-2 482671-44-3
482671-45-4 482671-46-5 482671-47-6 482671-48-7 482671-49-8
482671-50-1 482671-51-2 482671-52-3 482671-53-4 482671-54-5
482671-55-6 482671-56-7 482671-57-8 482671-58-9 482671-59-0
482671-60-3 482671-61-4 482671-62-5 482671-63-6 482671-64-7
482671-65-8 482671-66-9 482671-67-0
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; cancer cell cell-surface mol. and cancer-specific promoter identification, targeting complexes, binding partners, and treatment methods)

L42 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:5518 HCAPLUS
DOCUMENT NUMBER: 138:50824
TITLE: Gene-trap identification of host cell proteins required for hepatitis C **virus** replication
INVENTOR(S): Kolykhalov, Alexander Alexandrovich
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003004329	A1	20030102	US 2002-104398	20020322

PRIORITY APPLN. INFO.: US 2001-278157P P 20010323

AB The present invention relates to the field of antivirus therapy, esp. the treatment or prevention of hepatitis C virus (HCV). Provided are methods that facilitate the identification of host cell genes required for the replication of HCV. More specifically the methods allow to identify host cell proteins. Also provided are methods of identifying compds. that inhibit the activity(ies) of products of these genes required for HCV replication in host cells, and that therefore inhibit HCV replication. These compds. are useful as HCV antiviral pharmaceutical agents to treat or prevent HCV infections in humans. Also provided are novel host cell genes identified by these methods; HCV replicons comprising both a pos. and a neg. selectable marker gene; and cell lines comprising said replicons.

IC ICM A61K031-00
ICS C12Q001-70; C07H021-04; C12N015-09; C12N015-70; C12N015-74;

replication)
IT Transformation, genetic
(of host cell with transposon or retroviral construct; gene-trap identification of host cell proteins required for hepatitis C **virus** replication)
IT Genetic engineering
(of transposon and retroviral constructs; gene-trap identification of host cell proteins required for hepatitis C **virus** replication)
IT Genetic element
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(origin of replication, for bacterial replication; gene-trap identification of host cell proteins required for hepatitis C **virus** replication)
IT Genetic element
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyadenylation **signal**; gene-**trap** identification of host cell proteins required for hepatitis C **virus** replication)
IT RNA formation
(replication; gene-trap identification of host cell proteins required for hepatitis C **virus** replication)
IT Genetic element
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(splice acceptor **signal**, required for construct integration into host cell; gene-**trap** identification of host cell proteins required for hepatitis C **virus** replication)
IT Replicon
(suicidal HCV replicon introduction into host cell; gene-trap identification of host cell proteins required for hepatitis C **virus** replication)
IT Genetic element
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(terminator, construct component; gene-trap identification of host cell proteins required for hepatitis C **virus** replication)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tk, marker gene; gene-trap identification of host cell proteins required for hepatitis C **virus** replication)

L42 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:814667 HCAPLUS
DOCUMENT NUMBER: 137:324217
TITLE: Recombinant adenovirus expressing multiple mutant HIV antigens and immunostimulatory cytokine for use as genetic vaccine against human immunodeficiency **virus** infection
INVENTOR(S): Wang, Danher
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of Appl. No. PCT/US01/18238.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002155127	A1	20021024	US 2001-3035	20011101
WO 2001091536	A2	20011206	WO 2001-US18238	20010604
WO 2001091536	A3	20020808		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-585599 A2 20000602
WO 2001-US18238 A2 20010604

AB Recombinant adenovirus and methods of administration to a host are provided for eliciting immune response of the host to human immunodeficiency virus (HIV). The recombinant adenovirus is capable of expressing multiple wild type or mutant HIV antigens such as HIV envelope proteins without the cleavage site or the cytosolic domain, structural proteins such as Gag and its proteolytic fragments in a natural, secreted or membrane-bound form, and regulatory proteins such as Tat, Rev and Nef. Immuno-stimulators such as cytokines can also be expressed by the recombinant adenovirus to further enhance the immunogenicity of the HIV antigens.

IC ICM A61K039-12
ICS C12N007-00; A61K039-295; A61K039-21; A61K039-23; A61K039-235; C12N007-01; C12N015-00; C12N015-09; C12N015-63; C12N015-70; C12N015-74

NCL 424199100

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 63

IT Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(E6; recombinant adenovirus expressing multiple mutant HIV antigens and immunostimulatory cytokine for use as genetic vaccine against human immunodeficiency **virus** infection)

IT Transcription factors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(E7; recombinant adenovirus expressing multiple mutant HIV antigens and immunostimulatory cytokine for use as genetic vaccine against human immunodeficiency **virus** infection)

IT Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(F; recombinant adenovirus expressing multiple mutant HIV antigens and immunostimulatory cytokine for use as genetic vaccine against human immunodeficiency **virus** infection)

IT Glycoproteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

TITLE: Engineered **viruses** to select genes encoding **secreted** and **membrane**-bound **proteins** in mammalian cells
AUTHOR(S): Moffatt, Pierre; Salois, Patrick; Gaumond, Marie-Helene; St-Amant, Natalie; Godin, Eric; Lanctot, Christian
CORPORATE SOURCE: 416 de Maisonneuve West, Phenogene Therapeutics, Suite 1020, Montreal, QC, H3A 1L2, Can.
SOURCE: Nucleic Acids Research (2002), 30(19), 4285-4294
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have developed a functional genomics tool to identify the subset of cDNAs encoding secreted and membrane-bound proteins within a library (the secretome'). A **Sindbis virus** replicon was engineered such that the envelope protein precursor no longer enters the secretory pathway. cDNA fragments were fused to the mutant precursor and expression screened for their ability to restore membrane localization of envelope proteins. In this way, recombinant replicons were released within infectious viral particles only if the cDNA fragment they contain encodes a secretory signal. By using engineered viral replicons to selectively export cDNAs of interest in the culture medium, the methodol. reported here efficiently filters genetic information in mammalian cells without the need to select individual clones. This adaptation of the **signal trap**' strategy is highly sensitive (1/200 000) and efficient. Indeed, of the 2546 inserts that were retrieved after screening various libraries, more than 97% contained a putative signal peptide. These 2473 clones encoded 419 unique cDNAs, of which 77% were previously annotated. Of the 94 cDNAs encoding proteins of unknown function, 24% either had no match in databases or contained a secretory signal that could not be predicted from electronic data.
CC 3 (Biochemical Genetics)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:778096 HCAPLUS
DOCUMENT NUMBER: 137:289890
TITLE: DART conjugates of proteins and **nucleic acids** for use as analytical and therapeutic tools
INVENTOR(S): Roberts, Radclyffe L.; De Figueiredo, Paul
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 205 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079393	A2	20021010	WO 2002-US10566	20020402
WO 2002079393	C2	20021114		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-281133P P 20010402
US 2001-281342P P 20010403

AB The present invention provides Dynamic Action Ref. Tools, or DARTs, and methods of making and using DARTs. DARTs are conjugates of three moieties: a DART includes a Mol. Shaft covalently linked to a Linkage Polypeptide that is covalently linked to a Mol. Point. that can be used to detect a protein or nucleic acid analyte and that signal detection by a function of either the protein or the nucleic acid component of the conjugate. One of the components may be an affinity group such as an antigen or antibody, a second component is a nucleic acid that may be a probe sequence or a nucleic acid enzyme or a linker between two proteins. The oligonucleotide may contain functional elements or protein or enzyme recognition sites. The third component may be a second protein such as a reporter enzyme. The combination of protein and nucleic acid specificities and activities allows DARTs to be used in a wide range of applications. DARTs can be used, for example, for the isolation and anal. of nucleic acids, polypeptides, and the like, for regulating biol. activities and investigating inter-mol. interactions, and the like. DARTs, and DART libraries, can be formed and manipulated in vivo or in vitro. DARTs can be purified, and portions of DARTs can be exchanged with portions of other DARTs.

IC ICM C12N
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 9
ST DART dynamic action ref tool; protein **oligonucleotide** conjugate analytical reagent
IT Plasmids
(51, **DNA** relaxing enzyme of, conjugates; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT Plasmids
(61B4-K98, **DNA** relaxing enzyme of, conjugates; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT Magnetic particles
Microtiter plates
(DART nucleoproteins immobilized on; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT Fluoropolymers, uses
Glass, uses
Polyamides, uses
RL: DEV (Device component use); USES (Uses)
(DART nucleoproteins immobilized on; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT Microarray technology
(DARTboard; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT Nucleoproteins
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DARTs (Dynamic Action Ref. Tools); DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT Plasmids
(**DNA** relaxing enzyme of, conjugates; DART conjugates of

therapeutic tools)
IT 7440-21-3, Silicon, uses 9004-70-0, Nitrocellulose 24937-79-9, PVDF
RL: DEV (Device component use); USES (Uses)
(DART nucleoproteins immobilized on; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT 52350-85-3, Integrase
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene int, conjugates; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT 9001-99-4, RNase 9050-76-4, RNase H
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleoprotein conjugates, as reporter; DART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT 467518-45-2 467518-46-3 467518-47-4 467518-48-5 467518-49-6
467518-51-0 467518-52-1 467518-53-2 467518-54-3 467518-55-4
467518-56-5 467518-57-6 467518-58-7 467518-59-8 467518-60-1
467518-61-2 467518-62-3 467518-63-4
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; dART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT 467518-37-2 467518-38-3 467518-39-4 467518-40-7 467518-41-8
467518-42-9 467518-43-0 467518-44-1 467518-50-9
RL: PRP (Properties)
(unclaimed protein sequence; dART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)
IT 95088-49-6 122024-47-9 468056-62-4 468056-63-5 468056-64-6
468056-65-7 468056-66-8 468056-67-9 468056-68-0 468056-69-1
468056-70-4 468056-71-5 468056-72-6 468056-73-7 468056-74-8
468056-75-9 468056-76-0 468056-77-1 468056-78-2
RL: PRP (Properties)
(unclaimed sequence; dART conjugates of proteins and **nucleic acids** for use as anal. and therapeutic tools)

L42 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:634334 HCAPLUS
DOCUMENT NUMBER: 137:180775
TITLE: Influenza **viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of fowl plague **virus** and uses for gene therapy and vaccination
INVENTOR(S): Hobom, Gerd; Menke, Anette
PATENT ASSIGNEE(S): Artemis Pharmaceuticals Gmbh, Germany
SOURCE: Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1233059	A1	20020821	EP 2001-103060	20010209

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

WO 2002064757 A2 20020822 WO 2002-EP1257 20020207
WO 2002064757 A3 20021205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: EP 2001-103060 A 20010209

AB The present invention provides human influenza viruses comprising an RNA sequence encoding a modified RNA-polymerase (RNAP). It was found that specific modifications of the RNA sequence encoding the RNAP, in particular the RNAP PB1 subunit - so as to code for a polypeptide having a higher similarity with fowl plague virus strain Bratislava (FPV) RNAP - provides viruses capable of recognition of viral RNA (vRNA) promoter sequence variations (the so called promoter-up variants) leading to an increase in transcription and/or replication initiation rates. The vRNA promoter may comprise the modifications G3A and C8U, or G3C and C8G, preferably G3A, U5C and C8U, or G3C, U5C and C8G in the 3'-terminal region (5'-CCUGUUUCUACU-3' or 5'-CCUGUUUUUACU-3'); and the modifications U3A and A8U in the 5'-terminal region (5'-AGAAGAAUCAAGG-3'). The present invention also provides a process for the prepn. thereof, pharmaceutical compns. comprising said human influenza viruses and their use for gene transfer into mammalian cells, for ex vivo gene transfer into antigen-presenting cells, such as dendritic cells, for in vivo somatic gene therapy, or in vivo vaccination purposes. The invention also relates to other non-avian influenza viruses, including equine, porcine influenza viruses.

IC ICM C12N007-00
ICS C12N015-86; C07K014-11; A61K035-76; A61K039-145

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 10, 15

ST influenza **virus** vector modified RNA polymerase sequence; transcription replication influenza **virus** vector modified RNA polymerase; fowl plague **virus** RNA polymerase transcription replication modified promoter; vaccination gene therapy immunotherapy influenza **virus** vector

IT Viral RNA
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(2, encoding PB1 subunit of RNAP; influenza **viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of FPV and uses for gene therapy and vaccination)

IT Borna disease **virus**
(BDV, glycoprotein antigen from, incorporated in influenza virion envelopes; influenza **viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of FPV and uses for gene therapy and vaccination)

IT Proteins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(E6, from HPV, incorporated in influenza virion envelopes; influenza **viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of FPV and uses for gene therapy and vaccination)

IT Transcription factors

study); USES (Uses)
(**nucleotide** sequence; influenza **viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of FPV and uses for gene therapy and vaccination)

IT 449225-50-7 449225-51-8 449225-52-9 449225-53-0 449225-54-1
449225-55-2 449225-56-3 449225-57-4 449225-58-5 449225-59-6
449225-60-9
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; influenza **viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of fowl plague **virus** and uses for gene therapy and vaccination)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 8 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:539716 HCAPLUS
DOCUMENT NUMBER: 137:104775
TITLE: Methods for synthesis of proteins on spore or bacteriophage on surface of bacteria or fungi
INVENTOR(S): Pan, Jae Gu; Choi, Soo Keun; Jung, Heung Chae
PATENT ASSIGNEE(S): Genofocus Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055561	A1	20020718	WO 2002-KR59	20020115

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: KR 2001-2156 A 20010115

AB The present invention relates to methods for prepg. a protein of interest surface-displayed on genetic carrier, for improving a protein of interest, for isolating a substance of interest, bioconversion and producing antibodies. More particularly, the present invention relates to a method for prepg. a protein of interest surface-displayed on genetic carrier, which comprises transforming a host cell, harboring the genetic carrier selected from the group consisting of spore and virus, with a vector contg. a gene encoding the protein of interest, culturing the transformed host cell and expressing the protein of interest in the host cell and allowing a noncovalent bond to form between the expressed protein and a surface of the genetic carrier so that the protein of interest is displayed on the surface of the genetic carrier.

IC ICM C07K017-02
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 6, 7, 10, 15, 63
ST spore bacteriophage surface **protein** display cloning mutagenesis expression; **fusion protein** gene library spore

spore resistance to, selection using; methods for synthesis of proteins on spore or bacteriophage on surface of bacteria or fungi)

IT 442701-96-4 442701-97-5 442701-98-6 442701-99-7 442702-00-3
442702-01-4 442702-02-5, 7: PN: WO02055561 SEQID: 7 unclaimed
DNA 442702-04-7, 9: PN: WO02055561 SEQID: 9 unclaimed
DNA 442702-05-8
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; methods for synthesis of proteins on spore or bacteriophage on surface of bacteria or fungi)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 9 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:425354 HCAPLUS
DOCUMENT NUMBER: 137:2729
TITLE: Interaction trap systems for detecting protein interactions
INVENTOR(S): Brent, Roger; McCoy, John M.; Jessen, Timm H.; Xu, Chanxing Wilson
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: U.S., 30 pp., Cont.-in-part of U. S. 6,004,746.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6399296	B1	20020604	US 1996-630052	19960409
US 6004746	A	19991221	US 1995-504538	19950720
WO 9738127	A1	19971016	WO 1997-US5793	19970409
W: JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 904402	A1	19990331	EP 1997-917897	19970409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000508174	T2	20000704	JP 1997-536441	19970409

PRIORITY APPLN. INFO.:
US 1994-278082 A2 19940720
US 1995-504538 A2 19950720
US 1996-630052 A 19960409
WO 1997-US5793 W 19970409

AB Disclosed herein is a method of detg. whether a first protein is capable of phys. interacting with a second protein, involving: (a) providing a host cell which contains (i) a reporter gene operably linked to a protein binding site; (ii) a first fusion gene which expresses a first fusion protein, the first fusion protein including the first protein covalently bonded to a binding moiety which is capable of specifically binding to the protein binding site; and (iii) a second fusion gene which expresses a second fusion protein, the second fusion protein including the second protein covalently bonded to a gene activating moiety and being conformationally-constrained; and (b) measuring expression of the reporter gene as a measure of an interaction between the first and the second proteins. Also disclosed are methods for assaying protein interactions, and identifying antagonists and agonists of protein interactions. A thioredoxin interaction trap system was used with Cdk2 as bait in a yeast two-hybrid system to screen for interacting peptides. Growth on leucine-deficient medium was used in the first selection step. The largest colonies were streak purified and tested for the galactose-dependent expression of the LEU2 gene product and of .beta.-galactosidase. The strength of peptide binding to bait was judged

according to the intensity of the blue color produced by .beta.-galactosidase.

IC ICM C12Q001-68
ICS G01N033-53

NCL 435006000

CC 9-2 (Biochemical Methods)
Section cross-reference(s): 3, 6

IT Protein motifs
(NLS (nuclear localization **signal**), prey vector encoding fusion protein contg., of SV40; interaction **trap** systems for detecting protein interactions)

IT Simian **virus** 40
(prey vector encoding fusion protein contg. nuclear localization domain of; interaction trap systems for detecting protein interactions)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:332632 HCAPLUS
DOCUMENT NUMBER: 136:336197
TITLE: **Virus** like particles, their preparation and their use in drug screening and functional genomics
INVENTOR(S): Hunt, Nicholas
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of U.S. Ser. No. 673,257.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002052040	A1	20020502	US 2000-750185	20001229
WO 2001002551	A2	20010111	WO 2000-EP6144	20000626
WO 2001002551	A3	20011108		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

EP 1999-112451	A	19990630
EP 2000-106109	A	20000321
US 2000-191318P	P	20000321
EP 2000-110363	A	20000515
WO 2000-EP6144	W	20000626
US 2001-673257	A2	20011002
US 1999-141268P	P	19990630

AB The invention relates to virus like particles, their prepn. and their use preferably in pharmaceutical screening and functional genomics. The invention further provides a variety of assay formats to be used with said virus like particles. In a first aspect the invention provides a method to selectively incorporate or encapsulate proteinaceous target mols. into virus like particles (VLP5). Target mols. are co-expressed in recombinant cells together with signal mols. It is possible to generate a homogeneous

population of VLPs in which a functional target protein of choice is expressed either within the lipid bilayer of an enveloped VLP or within the capsid of a naked or enveloped VLP. It Is also possible to encapsulate target proteins within the VLP. These reactions are mediated by the specific interaction with a signaling protein. The incorporation/encapsulation of the resp. target proteins is preferably achieved by utilization of a signal mol. with a specific concatemeric protein sequence which interacts specifically and with high affinity with a complementary concatemeric tag located at either the carboxy or amino terminal end of the resp. target protein. When both of these modified proteins (signal and target) are expressed within the same host cell, then the expressed protein products assoc. with one another via the specific tags. This interaction results in a preferred embodiment in the translocation of the resp. complexes to the cell membrane in high concns. where they are extruded from the cells via a budding process similar to the release of mature virus particles. With respect to the second amino acid sequence of the signal mol., it is preferred that it comprises at least a fragment of a virus capsid or envelope protein, or a precursor of a virus capsid or envelope protein, or a mutant of a virus capsid or envelope protein. It is eg. also possible to utilize a second amino acid sequence of said signal mol. which is encoded by at least a fragment of a retrotransposon, in particular a Ty element in yeast, a copia element in insects, a copia-like element in insects, VL 30 in mice, or an IAP gene in mice. The invention is exemplified by displaying G-protein coupled receptors, or human epidermal growth factor receptor (EGFR), or endothelin receptors to allow identification of gene products interfering with protein-protein interactions within the cell.

IC ICM G01N033-53
ICS A61K039-12; C07K001-00; C07K017-00; C12N007-00; C12N007-01; C07K014-00
NCL 435235100
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 10, 13, 63
ST **virus** like particle prepn membrane protein interaction drug screening
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(SRE (serum-responsive element), as regulatory element; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Yeast
(Ty element of; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Transposable element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Ty element, signal mols. for VLPs encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Mouse
(VL30 element or IAP gene of; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(VL30 element, signal mols. for VLPs encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Cell membrane

WO 2002026995 A1 20020404 WO 2001-GB4131 20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2001087862 A5 20020408 AU 2001-87862 20010914
PRIORITY APPLN. INFO.: GB 2000-23910 A 20000929
GB 2000-23911 A 20000929
GB 2000-27693 A 20001113
WO 2001-GB4131 W 20010914

AB The present invention provides, inter alia, a glyphosate resistant EPSPS enzyme wherein in comparison with the wild type enzyme the EPSPS protein sequence is modified in that a first position is mutated so that the residue at this position is Ile rather that Thr and a second position is mutated so that the residue at this position is Ser rather than Pro, the mutations being introduced into EPSPS sequences which comprise the conserved region GNAGTAMRPL in the wild type enzyme such that modified sequence reads GNAGIAMRSL. The invention also includes glyphosate resistant plants regenerated from material transformed with polynucleotides which encode such EPSPS enzymes and a method of selectively controlling weeds in a field comprising such plants and glyphosate sensitive weeds, by the application to the field of glyphosate or an agronomically acceptable deriv.

IC ICM C12N015-54
ICS C12N015-82; C12N009-10; A01H005-00

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 11

IT Proteins
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(MP (movement protein), for **virus** resistance in transgenic plant; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT Proteins
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(coat, for **virus** resistance in transgenic plant; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT Cauliflower mosaic **virus**
Figwort mosaic **virus**
(enhancer of 35S promoter of; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT Antisense **oligonucleotides**
Ribozymes
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(for **virus** resistance in transgenic plant; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT **Signal peptides**
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)

(of EPSPS and Brassica napus of soybean; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT 37205-61-1, **Protease** inhibitor
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(cysteine-, in transgenic plant; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT 9013-09-6, Phosphoenolpyruvate synthase 9027-40-1, Pyruvate orthophosphate di-kinase
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(transit peptide of, **fusion protein** with; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT 407647-96-5, 1: PN: WO0226995 SEQID: 1 unclaimed **DNA**
407647-97-6 407647-98-7 407647-99-8 407648-00-4 407648-01-5
407648-02-6 407648-03-7 407648-04-8 407648-05-9 407648-06-0
407648-07-1 407648-08-2 407648-09-3 407648-10-6 407648-11-7
407648-12-8 407648-13-9 407648-14-0 407648-15-1 407648-16-2
407648-17-3 407648-18-4 407648-19-5 407648-20-8 407648-21-9
407648-22-0 407648-23-1 407648-24-2 407648-25-3 407648-26-4
407648-27-5 407648-28-6 407648-29-7 407648-30-0 407648-31-1
407648-32-2 407648-33-3 407648-34-4 407648-35-5 407648-36-6
407648-37-7 407648-38-8 407648-39-9 407648-40-2 407648-41-3
407648-42-4 407648-43-5 407648-44-6
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

IT 9031-50-9, Replicase
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(viral, for **virus** resistance in transgenic plant; mutagenesis of plant 5-enol pyruvyl shikimate phosphate synthetase for stable enzyme expression in transgenic plant for glyphosate resistant)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220335 HCAPLUS
DOCUMENT NUMBER: 136:261800
TITLE: Adenovirus vectors expressing gag, pol, and nef **fusion proteins** for use as HIV-1 vaccine
INVENTOR(S): Emini, Emilio A.; Youil, Rima; Bett, Andrew J.; Chen, Ling; Kaslow, David C.; Shiver, John W.; Toner, Timothy J.; Casimiro, Daniel R.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 257 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022080	A2	20020321	WO 2001-US28861	20010914

WO 2002022080 A3 20020502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2001094562 A5 20020326 AU 2001-94562 20010914
PRIORITY APPLN. INFO.: US 2000-233180P P 20000915
WO 2001-US28861 W 20010914

AB First generation adenoviral vectors and assocd. recombinant adenovirus-based HIV vaccines which show enhanced stability and growth properties and greater cellular-mediated immunity are described within this specification. These adenoviral vectors are utilized to generate and produce through cell culture various adenoviral-based HIV-1 vaccines which contain HIV-1 gag, HIV-1 pol and/or HIV-1 nef polynucleotide pharmaceutical products, and biol. relevant modifications thereof. These adenovirus vaccines, when directly introduced into living vertebrate tissue, preferably a mammalian host such as a human or a non-human mammal of com. or domestic veterinary importance, express the HIV1- Gag, Pol and/or Nef protein or biol. modification thereof, inducing a cellular immune response which specifically recognizes HIV-1. The exemplified polynucleotides of the present invention are synthetic DNA mols. encoding HIV-1 Gag, encoding codon optimized HIV-1 Pol, derivs. of optimized HIV-1 Pol (including constructs wherein protease, reverse transcriptase, RNAse H and integrase activity of HIV-1 Pol is inactivated), HIV-1 Nef and derivs. of optimized HIV-1 Nef, including nef mutants which effect wild type characteristics of Nef, such as myristylation and down regulation of host CD4. The adenoviral vaccines of the present invention, when administered alone or in a combined modality regime, will offer a prophylactic advantage to previously uninfected individuals and/or provide a therapeutic effect by reducing viral load levels within an infected individual, thus prolonging the asymptomatic phase of HIV-1 infection.

IC ICM A61K

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 63

IT Animal cell line
(293; adenovirus vector encoding **chimeric** gag, pol, and nef **proteins** for use as HIV-1 vaccine)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CAE (cis-acting element), packaging region; adenovirus vector encoding **chimeric** gag, pol, and nef **proteins** for use as HIV-1 vaccine)

IT Gene, microbial
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(E1; adenovirus vector encoding **chimeric** gag, pol, and nef **proteins** for use as HIV-1 vaccine)

IT Gene, microbial
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(E3; adenovirus vector encoding **chimeric** gag, pol, and nef **proteins** for use as HIV-1 vaccine)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IRES (internal ribosomal entry site) element; adenovirus vector

(unclaimed sequence; adenovirus vectors expressing gag, pol, and nef **fusion proteins** for use as HIV-1 vaccine)

L42 ANSWER 13 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:157962 HCAPLUS
DOCUMENT NUMBER: 136:195286
TITLE: Uses of **alphavirus** genome for screening **libraries** of exogenous **nucleic acids** and selecting a **nucleic acid** having a desired feature
INVENTOR(S): Lanctot, Christian; Moffat, Pierre; Salois, Patrick
PATENT ASSIGNEE(S): Phenogene Therapeutiques Inc., Can.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002016572	A2	20020228	WO 2001-CA1169	20010817
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001087396	A5	20020304	AU 2001-87396	20010817

PRIORITY APPLN. INFO.: US 2000-641931 A1 20000818
WO 2001-CA1169 W 20010817

AB This invention relates to the use of a virus or of a viral genome for screening/selecting exogenous nucleic acids having a desired feature. More particularly, the present invention provides a dysfunctional viral genome capable of both expressing libraries of exogenous nucleic acids and selecting the sequences having a predefined characteristic or function within the cell, such as as nucleic acids encoding **signal peptides**, secreted proteins, membrane bound proteins, proteases, protease cleaving site and drug-resistance proteins. The invention further provides methods and kits for selecting nucleic acids having a desired feature. According to one embodiment, prodn. of a viral particle is dependent on insertion of an exogenous nucleic acid having the desired feature into a dysfunctional viral genome or into a viral genome exposed to a substance inhibiting viral packaging function(s).

IC ICM C12N015-00
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 10
ST protein screening **nucleic acid library** **alphavirus** genome
IT Neurohormones
RL: ANT (Analyte); ANST (Analytical study)
(7B2; uses of **alphavirus** genome for screening **libraries** of exogenous **nucleic acids** and selecting a **nucleic acid** having a desired feature)
IT Cadherins
RL: ANT (Analyte); ANST (Analytical study)
(E-; uses of **alphavirus** genome for screening

401059-23-2, 5: PN: WO0216572 SEQID: 5 unclaimed **DNA**
401059-24-3, 6: PN: WO0216572 SEQID: 6 unclaimed **DNA**
401059-25-4, 7: PN: WO0216572 SEQID: 7 unclaimed **DNA**
401059-26-5, 8: PN: WO0216572 SEQID: 8 unclaimed **DNA**
401059-27-6, 9: PN: WO0216572 SEQID: 9 unclaimed **DNA**
401059-28-7 401059-29-8 401059-30-1 401059-31-2 401059-32-3
401059-33-4 401059-34-5 401059-35-6 401059-36-7 401059-37-8
401059-38-9 401059-39-0 401059-40-3 401059-41-4 401059-42-5
401059-43-6 401059-44-7 401059-45-8 401059-46-9 401059-47-0
401059-48-1 401059-49-2 401059-50-5
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; uses of **alphavirus** genome for screening **libraries** of exogenous **nucleic acids** and selecting a **nucleic acid** having a desired feature)

IT 401059-51-6 401059-53-8 401059-54-9 401059-55-0 401059-56-1
401059-57-2 401059-58-3 401059-59-4 401059-60-7 401059-61-8
401059-62-9 401059-63-0 401059-64-1 401059-65-2 401059-66-3
RL: PRP (Properties)
(unclaimed protein sequence; uses of **alphavirus** genome for screening **libraries** of exogenous **nucleic acids** and selecting a **nucleic acid** having a desired feature)

IT 401470-19-7
RL: PRP (Properties)
(unclaimed sequence; uses of **alphavirus** genome for screening **libraries** of exogenous **nucleic acids** and selecting a **nucleic acid** having a desired feature)

IT 9001-92-7, **Protease** 9032-64-8, **Nucleotide** pyrophosphatase 37318-49-3, Protein disulfide isomerase 65979-36-4, Signal peptidase 91448-99-6, Cystatin C 150523-26-5, IGF-BP-5 **protease**
RL: ANT (Analyte); ANST (Analytical study)
(uses of **alphavirus** genome for screening **libraries** of exogenous **nucleic acids** and selecting a **nucleic acid** having a desired feature)

IT 141760-45-4, Furin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(uses of **alphavirus** genome for screening **libraries** of exogenous **nucleic acids** and selecting a **nucleic acid** having a desired feature)

L42 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:713531 HCAPLUS
DOCUMENT NUMBER: 135:268120
TITLE: Use of promoterless reporter genes to elucidate protein expression profiles in cells by gene trapping
INVENTOR(S): Link, Charles J.; Seregina, Tatiana; Vahanian, Nicholas N.; Higginbotham, James N.; Ramsey, Jay W.; Powers, Bradley J.; Link, Sachet A.; Young, Won Bin
PATENT ASSIGNEE(S): Newlink Genetics, USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001070948 A2 20010927 WO 2001-US8770 20010319
WO 2001070948 A3 20020404
WO 2001070948 C2 20021219
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2001034028 A1 20011025 US 2001-811842 20010319
EP 1268767 A2 20030102 EP 2001-922469 20010319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2000-190678P P 20000320
US 2000-198722P P 20000420
WO 2001-US8770 W 20010319

AB The present invention relates generally to methods and compns. for the identification of differential protein expression patterns and concomitantly the active genetic regions that are directly or indirectly involved in different tissue types, disease states, or other cellular differences desirable for diagnosis or for targets for drug therapy. The method uses a promoterless reporter gene as an anal. tool. The reporter gene is delivered, along with a selectable marker into a host cell and integration is forced by selection. Patterns of expression of individual integration events can be monitored by following reporter gene expression. The reporter gene may include other elements such as polyadenylation sites or an internal ribosome entry site to improve levels of expression of the reporter moiety. The gene into which the reporter is integrated can be identified by rescue techniques.

IC ICM C12N015-10
ICS C12Q001-68

CC 3-1 (Biochemical Genetics)

IT Retroviral vectors
Virus vectors
(for delivery of promoterless reporter genes; use of promoterless reporter genes to elucidate protein expression profiles in cells by gene trapping)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyadenylation **signal**, in promoterless reporter constructs; use of promoterless reporter genes to elucidate protein expression profiles in cells by gene **trapping**)

IT Adeno-associated **virus**
Adenoviridae
Lentivirus
(vectors for delivery of promoterless reporter genes; use of promoterless reporter genes to elucidate protein expression profiles in cells by gene trapping)

L42 ANSWER 15 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:598026 HCAPLUS
DOCUMENT NUMBER: 135:179704
TITLE: Cytokine inhibitory molecules from tick salivary glands
INVENTOR(S): Fuchsberger, Norbert; Hajnicka, Valeria; Kocakova, Paula; Slovak, Mirko; Gasperik, Juraj

PATENT ASSIGNEE(S): Evolutec Ltd., UK
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058941	A1	20010816	WO 2001-GB536	20010209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1254168	A2	20021106	EP 2001-904133	20010209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: GB 2000-3245 A 20000211
GB 2000-31708 A 20001222
WO 2001-GB536 W 20010209

AB The present invention relates to cytokine activity regulator mols. (CARMs) and their use in controlling the action of cytokines, particularly chemokines. In particular, the invention relates to CARMs that are derived from parasite salivary glands. The invention also relates to the use of CARMs in the treatment of diseases and allergies and in the prodn. of vaccines that protect mammals, including humans, against the transmission of pathogenic (disease-causing) micro-organisms by certain parasites.

IC ICM C07K014-435
ICS C12N015-12; C12N005-10; C12Q001-68; A61K038-16; A61P037-06; A61K039-00

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 63

IT **DNA**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(double-stranded; macroparasite-derived cytokine inhibitory mols. for controlling action of cytokine or chemokine and for treating autoimmune diseases and allergies)

IT Gene
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**library**; macroparasite-derived cytokine inhibitory mols. for controlling action of cytokine or chemokine and for treating autoimmune diseases and allergies)

IT Allergy
Amblyomma variegatum
Atherosclerosis
Autoimmune disease
Blackfly
Dermacentor reticulatus
Epitopes
HPLC

Haemaphysalis inermis
Hookworm
Infection
Ixodes ricinus
Leech (Hirudinea)
Lyme disease
Malaria
Mammal (Mammalia)
Melanoma
Microorganism
Mite and Tick
Molecular cloning
Mosquito
Nairobi sheep disease **virus**
Osteoporosis
Pathogen
Psoriasis
Rheumatoid arthritis
Rhipicephalus appendiculatus
Salivary gland
Sandfly
Sepsis
Tabanidae
Vaccines
(macroparasite-derived cytokine inhibitory mols. for controlling action of cytokine or chemokine and for treating autoimmune diseases and allergies)

IT **Fusion proteins (chimeric proteins)**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macroparasite-derived cytokine inhibitory mols. for controlling action of cytokine or chemokine and for treating autoimmune diseases and allergies)

IT **cDNA**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macroparasite-derived cytokine inhibitory mols. for controlling action of cytokine or chemokine and for treating autoimmune diseases and allergies)

IT **Signal peptides**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(secretion; macroparasite-derived cytokine inhibitory mols. for controlling action of cytokine or chemokine and for treating autoimmune diseases and allergies)

IT **Nucleic acids**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthetic; macroparasite-derived cytokine inhibitory mols. for controlling action of cytokine or chemokine and for treating autoimmune diseases and allergies)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 16 OF 33 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:545860 HCAPLUS
DOCUMENT NUMBER: 135:151618
TITLE: Cloning of **cDNAs** for tumor-assocd. antigens and use in cancer diagnosis and therapy thereof
INVENTOR(S): Ashkenazi, Avi J.; Goddard, Audrey; Godowski, Paul J.; Gurney, Austin L.; Hillan, Kenneth J.; Marsters, Scot A.; Pan, James; Pitti, Robert M.; Roy, Margaret Ann; Smith, Victoria; Stone, Donna M.; Watanabe, Colin K.; Wood, William I.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 302 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 114
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053486	A1	20010726	WO 2000-US3565	20000211
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 9946281	A2	19990916	WO 1999-US5028	19990308
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 9963088	A2	19991209	WO 1999-US12252	19990602
WO 9963088	A3	20010329		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2000012708	A2	20000309	WO 1999-US20111	19990901
WO 2000012708	A3	20011004		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				

(gene therapy of HIV-pos. patients involving expression of membrane-anchored gp41 peptides)
IT Hematopoietic precursor cell
(stem, **transfection** of; gene therapy of HIV-pos. patients involving expression of membrane-anchored gp41 peptides)
IT T cell (lymphocyte)
(**transfection** of; gene therapy of HIV-pos. patients involving expression of membrane-anchored gp41 peptides)
IT 342859-83-0P
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(**nucleotide** sequence; gene therapy of HIV-pos. patients involving expression of membrane-anchored gp41 peptides)
IT 342868-79-5, 3: PN: WO0137881 SEQID: 3 unclaimed **DNA**
342868-80-8 342868-81-9 342868-82-0 342868-83-1 342868-84-2
342868-85-3 342868-86-4 342868-87-5 342868-88-6 342868-89-7
342868-90-0
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; gene therapy of HIV-pos. patients by the expression of membrane-anchored gp41 peptides)

L42 ANSWER 20 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:380649 HCAPLUS
DOCUMENT NUMBER: 135:4472
TITLE: Antigen-binding fragments specific for dendritic cells, compositions and methods of use thereof antigens recognized thereby and cells obtained thereby
INVENTOR(S): Schmitz, Juergen; Dzionek, Andrzej; Buck, David William
PATENT ASSIGNEE(S): Miltenyi Biotech G.m.b.H., Germany
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036487	A2	20010525	WO 2000-IB1832	20001115
WO 2001036487	A3	20020510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 1999-165555P	P	19991115
US 1999-167076P	P	19991123
US 2000-179003P	P	20000128
US 2000-180775P	P	20000207
US 2000-196824P	P	20000411
US 2000-197205P	P	20000413

AB The invention provides antigen-binding fragments specific for dendritic cells and effective in treatment and/or diagnosing a variety of disorders. Methods of use are also provided as are methods for screening for addnl. such antigen-binding fragments and the products obtained thereby.

IC ICM C07K016-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 3, 9, 63
IT Allergy
Anaphylaxis
Animal tissue culture
Animal **virus**
Antitumor agents
Arthritis
Asthma
Autoimmune disease
Bacteria (Eubacteria)
Cell fusion
Chemiluminescent substances
Cord blood
Cytomegalovirus
Dendritic cell
Dermatomyositis
Drug screening
Drugs
Epitopes
Fluorescent substances
Fungi
Hepatitis
Herpesviridae
Human immunodeficiency **virus**
Immune tolerance
Inflammation
Influenza
Labels
Lentivirus
Leukemia
Lupus erythematosus
Melanoma
Molecular cloning
Multiple myeloma
Multiple sclerosis
Mycosis
Newborn
Nucleic acid hybridization
Phage display **library**
Protein sequences
Pseudomonas
Psoriasis
Rheumatoid arthritis
Rhinovirus
Sjogren's syndrome
Testis, neoplasm
Transplant and Transplantation
Transplant rejection
Urticaria
cDNA sequences
(antibody fragments specific for antigen BDCAs for treatment and diagnosis of dendritic cell-assocd. diseases such as inflammation and cancer)
IT **Fusion proteins (chimeric proteins**
)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody fragments specific for antigen BDCAs for treatment and

diagnosis of dendritic cell-assocd. diseases such as inflammation and cancer)

IT **Signal peptides**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody fragments specific for antigen BDCAs for treatment and diagnosis of dendritic cell-assocd. diseases such as inflammation and cancer)

IT 342058-86-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**nucleotide** sequence; antibody fragments specific for antigen BDCAs for treatment and diagnosis of dendritic cell-assocd. diseases such as inflammation and cancer)

IT 342059-20-5 342059-21-6
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; antigen-binding fragments specific for dendritic cells, compns. and methods of use thereof antigens recognized thereby and cells obtained thereby)

L42 ANSWER 21 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:31664 HCAPLUS
DOCUMENT NUMBER: 134:96215
TITLE: Method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs
INVENTOR(S): Frisch, Christian; Kretzschmar, Titus; Hoss, Adolf; Von Ruden, Thomas
PATENT ASSIGNEE(S): Morphosys A.-G., Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002588	A2	20010111	WO 2000-EP6137	20000630
WO 2001002588	A3	20010712		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2339889	AA	20010111	CA 2000-2339889	20000630
EP 1133565	A2	20010919	EP 2000-947904	20000630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2003504031	T2	20030204	JP 2001-508360	20000630

PRIORITY APPLN. INFO.: EP 1999-112815 A 19990702
WO 2000-EP6137 W 20000630

AB The present invention provides methods for generation of specific binding partners binding to (poly)peptides encoded by genomic DNA fragments or ESTs. The (poly)peptides are expressed as part of fusion proteins which are forming inclusion bodies on expression in host cells. The inclusion bodies are used to generate binding partners which bind specifically to said (poly)peptides. The specific binding partners, in particular Igs or fragments thereof, are useful for anal. and functional characterization of proteins encoded by nucleic acid sequences comprising the corresponding genomic DNA fragments or ESTs. The invention further relates to nucleic acid mols., vectors and host cells to be used in the methods of the

present invention. The invention further relates to the use of fusion proteins comprising the first N-terminal domain of the gene III protein of filamentous phage as fusion partner for the expression of a (poly)peptide/protein fused to said fusion partner, and to methods for the expression of (poly)peptide/proteins.

IC ICM C12N015-62
ICS C07K016-00; C12N001-21; C12N015-70; C12N005-10; C12N001-19; C07K014-705; C07K014-045

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 9

ST **chimeric protein** binding EST **DNA** sequence filamentous phage

IT Thioredoxins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(E. coli, as fusion partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Eukaryote (Eukaryotae)
Prokaryote
(EST and genomic **DNA** fragments from, as host; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Animal
Mammal (Mammalia)
Pathogen
Virus
(EST and genomic **DNA** fragments from; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Peptide **library**
(Ig; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(MBP (maltose-binding **protein**), E. coli, as **fusion** partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT **Fusion proteins** (**chimeric proteins**)
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-terminal domain of the geneIII **protein** of filamentous phage as **fusion** partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(as fusion partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Bacteria (Eubacteria)
Escherichia coli
Insect (Insecta)
(as host; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT EST (expressed sequence tag)

RL: ANT (Analyte); ANST (Analytical study)
(**cDNA** with; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Cytoplasm
(cytosol, **chimeric protein** expressed in; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Bacteriophage
(filamentous; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Disulfide group
(fusion partner comprising; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(g3p; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(geneIII, as **fusion** partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT **DNA**
RL: ANT (Analyte); ANST (Analytical study)
(genomic; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linker, comprising a cleavage **signal**; method for generation of specific binding partners binding to (poly)**peptides** encoded by genomic **DNA** fragments or ESTs)

IT Molecular cloning
Phage display **library**
(method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Genetic vectors
(pBAD-N1-MCS-H; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Genetic vectors
(pTFT74-N1-MCS-H; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Interferons
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(porcine, as fusion partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT Conformation
(protein; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(secretory, as **fusion** partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT 9001-78-9, Alkaline phosphatase 9013-93-8, Phospholipase 9073-60-3, .beta.-Lactamase 9075-06-3, RNAse II
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(E. coli, as fusion partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT 9012-90-2, **DNA** polymerase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(T5, as fusion partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT 176742-42-0, Procathepsins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(human, as fusion partner; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT 319934-78-6, 1: PN: WO0102588 PAGE: 18 unclaimed **DNA**
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

IT 318450-35-0 319934-79-7 319934-80-0 319934-81-1 319934-82-2 319934-83-3
RL: PRP (Properties)
(unclaimed sequence; method for generation of specific binding partners binding to (poly)peptides encoded by genomic **DNA** fragments or ESTs)

L42 ANSWER 22 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:31628 HCAPLUS
DOCUMENT NUMBER: 134:96212
TITLE: **Virus** like particles, their preparation and their use preferably in pharmaceutical screening and functional genomics
INVENTOR(S): Hunt, Nicholas
PATENT ASSIGNEE(S): Evotec Biosystems A.-G., Germany
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002551	A2	20010111	WO 2000-EP6144	20000626
WO 2001002551	A3	20011108		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1187928 A2 20020320 EP 2000-949236 20000630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2003504014 T2 20030204 JP 2001-508324 20000630
US 2002052040 A1 20020502 US 2000-750185 20001229
EP 1219705 A1 20020703 EP 2000-128686 20001229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: EP 1999-112451 A 19990630
US 1999-141268P P 19990630
EP 2000-106109 A 20000321
EP 2000-110363 A 20000515
US 2000-191318P P 20000321
WO 2000-EP6144 W 20000626
US 2001-673257 A2 20011002

AB The invention relates to virus like particles (VLP), their prepn. and their use in pharmaceutical screening and functional genomics. The VLP can display the target protein within the its capsid through either strong specific interaction of a mol. peptide tag covalently attached to the C-terminus of the signal protein (Gag) with a complementary specific peptide tag assocd. with the target of interest or by direct covalent fusion of the Gag protein with the target protein/peptide of interest. The Gag-tag fusion protein is co-expressed in a cellular system with the resp. mol. of interest which also carries a specific peptide tag either within the mol. or at either the N- or C-terminus. Expression of the modified Gag protein in the resp. host cells results in the accumulation of the Gag protein at the plasma membrane due to signals present within the N-terminal portion of the Gag protein. High concns. of this protein at the plasma membrane results in a budding process in which VLPs are released into the extracellular milieu. If the target protein carrying the complementary tag is expressed in the same cell and is concd. in the intracellular compartments then the specific interaction with the tagged Gag protein results in the cotransport of the target to the plasma membrane and subsequent incorporation into the released VLPs. The invention further provides a variety of assay formats to be used with said virus like particles. The invention is exemplified by displaying G-protein coupled receptors, or human epidermal growth factor receptor (EGFR), or endothelin receptors to allow identification of gene products interfering with protein-protein interactions within the cell.

IC ICM C12N015-00
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 10, 13, 63
ST **virus** like particle prepn membrane protein interaction drug screening

IT Codons
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(ATG, substitution for **fusion protein** prepn.; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Endothelin receptors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(ETA; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(SRE (serum-responsive element), as regulatory element; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Yeast
(Ty element of; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Transposable element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Ty element, signal mols. for VLPs encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Mouse
(VL30 element or IAP gene of; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(VL30 element, signal mols. for VLPs encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Cell membrane
Endoplasmic reticulum
Golgi apparatus
(VLPs released through budding from; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Exocytosis
(VLPs released through; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Fluorometry
(anisotropy measurements, for VLP detection; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Cell adhesion molecules
Enzymes, biological studies
G protein-coupled receptors
Ion channel
Nuclear receptors
Receptors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(as VLPs displaying target; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Protein motifs
(binding domain, interaction with; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Bacteriophage
Baculoviridae
Coronavirus
Hepadnaviridae
Herpesviridae
Nodavirus
Papillomavirus
Parvovirus
Picornaviridae
Polyomavirus

Reoviridae
Retroviridae
(capsid or envelope protein derived from; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Virion structure
(capsid, VLP target protein incorporated into; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(capsid, in VLPs; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Proteins, general, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cell surface; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Insect (Insecta)
(copia element of; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Retrotransposon
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(copia, signal mols. for VLPs encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Fluorometry
(correlation or cross-correlation, for VLP detection; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Test kits
(corresponding VLPs; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cyclic adenosine monophosphate responsive elements; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Cytoplasm
(cytosol, receptors, as VLPs displaying target; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Genomic **library**
Peptide **library**
cDNA library
(drug screened from; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Antisense **DNA**
Nucleic acids
Peptide **nucleic acids**
cDNA
mRNA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(drug screened from; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Autoimmune disease

Neoplasm
(drug screening for; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Virion structure
(envelope; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Confocal laser scanning microscopy
Dielectrophoresis
Electric impedance
Light scattering
Microscopy
Resonance fluorescence
Spectroscopy
(for VLP detection; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Enzymes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for VLP target protein labeling and detection; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Genetic vectors
(for drug screening; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Reporter gene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for drug screening; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Luminescence, bioluminescence
(for peptides or protein labeling; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gag, encoding structural proteins for VLP; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Disease, animal
(genetic, drug screening for; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(green fluorescent, luminescent; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Genetic methods
(homogeneous high throughput assay; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(iap, signal mols. for VLPs encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Myristoylation
(inactivation by removing methionine in protein; **virus** like particles, prepn. and use preferably in pharmaceutical screening and

functional genomics)
IT Animal cell
(infection, drug screening for; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Fluorometry
(intensity distribution, for VLP detection; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Hydrogen bond
Steric effects
(interaction through; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Ligands
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interaction with binding domain; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Biological transport
(intracellular, protein assocd. with; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Second messenger system
Signal transduction, biological
(intracellular; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Fluorometry
(lifetime measurements, for VLP detection; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Peptides, biological studies
Proteins, general, biological studies
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(luminescent; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(membrane, functional integral; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Cell nucleus
(membrane; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Electrostatic force
Van der Waals force
(noncovalent interaction through; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Membrane, biological
(nuclear; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT **Fusion proteins (chimeric proteins)**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(of VLP target **protein** and **virus** capsid or envelope **proteins**; **virus** like particles, prepn. and use

preferably in pharmaceutical screening and functional genomics)
IT Envelope proteins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(of **virus**; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Cell membrane
(pores, components as VLPs displaying target; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Animal cell
(recombinant; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulatory; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(responsive to intracellular calcium ion; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Translation, genetic
(signal mol.; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Retrotransposon
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal mols. for VLPs encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Molecular association
(stacking interactions, noncovalent interaction through; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(structural, as signal mols. for VLPs; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Retrotransposon
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(translational signal mol. encoded by; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(transmembrane, receptors, as VLPs displaying target; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Diagnosis
(using VLPs; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)
IT Animal **virus**

Drug screening
Drugs
Signal transduction, biological
Transcriptional regulation
(**virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT **Signal peptides**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT Encapsulation
(**virus**; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

IT 14127-61-8, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(regulatory element responsive to; **virus** like particles, prepn. and use preferably in pharmaceutical screening and functional genomics)

L42 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:310162 HCAPLUS
DOCUMENT NUMBER: 134:96008
TITLE: Cloning of novel chemokines using a **signal** sequence **trap** method
AUTHOR(S): Imai, Toshio
CORPORATE SOURCE: Department of Microbiology, Kinki University School of Medicine, Osaka, Japan
SOURCE: Methods in Molecular Biology (Totowa, New Jersey) (2000), 138(Chemokine Protocols), 11-21
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An efficient **signal** sequence **trap** method based on the Epstein-Barr **virus** shuttle vector pDREF-CD4ST is described. The **signal** sequences **trap** takes advantage of the presence of N-terminal signal sequences in most precursor forms of secretory and transmembrane proteins, including chemokines. Protocols include: synthesis of 5' portion-enriched cDNA; construction of the **signal** sequence **trap** library; and cloning and isolation of signal sequence-encoding cDNAs.

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 15

ST chemokine cloning **signal** sequence **trap** method

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cloning of novel chemokines using a **signal** sequence **trap** method)

IT cDNA
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(in **signal** sequence **trap** method for cloning **secreted** and cell surface **proteins**)

IT Molecular cloning
(**signal** sequence **trap** method for cloning **secreted** and cell surface **proteins**)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

using HIV-1 p24 as epitope for tagging)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 25 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:36412 HCAPLUS
DOCUMENT NUMBER: 128:71252
TITLE: Development of a nuclear export **signal trapping** method for isolating genes with HIV Rev activity
AUTHOR(S): Zhang, Ming Jie; Dayton, Andrew I.
CORPORATE SOURCE: Lab. Molecular Virology, Div. Transfusion-Transmitted Diseases, Center Biologics Evaluation Res., Food Drug Administration, Rockville, MD, 20852, USA
SOURCE: Journal of Biomedical Science (Basel) (1997), 4(6), 289-294
CODEN: JBCIEA; ISSN: 1021-7770
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have developed a method for nuclear export **signal trapping** (NEST) to isolate functional Rev clones from various types of libraries such as libraries of Rev mutants. The expression libraries are cotransfected into COS cells together with a novel Rev-dependent immunoselectable CD28 expression plasmid, pCMV128-CD28. CD28-pos. cells are recovered by fluorescence-activated cell sorting or by immune pptn. with magnetic beads, and the low-mol.-wt. extra chromosomal DNA is recovered, amplified for Rev-contg. DNA by PCR and recloned into expression plasmids. The resulting clones are enriched for functional Rev clones. These can be recovered efficiently after several repetitive NEST cycles. This technique may be usefully applied to study various regions of Rev, such as the RNA binding domain and the nuclear export signal, or effector domain and potentially to the isolation of cellular factors with nuclear export capabilities.
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 10, 15
ST rev gene nuclear export **signal trapping**
IT Cytometry
(FACS (fluorescence-activated cell sorting); a nuclear export **signal trapping** method for isolating genes with HIV Rev activity)
IT Protein motifs
(NES (nuclear export **signal**); a nuclear export **signal trapping** method for isolating genes with HIV Rev activity)
IT Human immunodeficiency **virus**
(a nuclear export **signal trapping** method for isolating genes with HIV Rev activity)
IT CD28 (antigen)
Rev protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a nuclear export **signal trapping** method for isolating genes with HIV Rev activity)
IT Biological transport
(export; a nuclear export **signal trapping** method for isolating genes with HIV Rev activity)
IT Immunoassay
(immunopptn.; a nuclear export **signal trapping** method for isolating genes with HIV Rev activity)
IT Plasmids
(pCMV128-CD28; a nuclear export **signal trapping**

method for isolating genes with HIV Rev activity)

L42 ANSWER 26 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:506783 HCAPLUS
DOCUMENT NUMBER: 127:148353
TITLE: Effector cell activation via chimeric receptors : **DNA** delivery process and therapeutic potential
INVENTOR(S): Bebbington, Christopher Robert; Lawson, Alastair David Griffiths; Weir, Andrew Neil Charles; Finney, Helene Margaret
PATENT ASSIGNEE(S): Celltech Therapeutics Ltd., UK; Bebbington, Christopher Robert; Lawson, Alastair David Griffiths; Weir, Andrew Neil Charles; Finney, Helene Margaret
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723613	A2	19970703	WO 1996-GB3209	19961223
WO 9723613	A3	19970821		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2238873	AA	19970703	CA 1996-2238873	19961223
AU 9712019	A1	19970717	AU 1997-12019	19961223
AU 729757	B2	20010208		
EP 870019	A2	19981014	EP 1996-943229	19961223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000502562	T2	20000307	JP 1997-523428	19961223

PRIORITY APPLN. INFO.: GB 1995-26131 A 19951221
WO 1996-GB3209 W 19961223

AB A cell activation process is described in which an effector cell is transformed with DNA coding for a chimeric receptor contg. two or more different cytoplasmic signaling components. For example, a single-chain Fv fragment of a humanized antibody was fused to a hinge region fragment of IgG1 and a transmembrane and/or cytoplasmic fragment of CD28 and CD3.zeta.. The resulting fusion protein, when transfected into mouse T-cells, was found to direct effector activity against the HL-60 cell line. Thus, the activated cell(s) maybe of use in medicine for example in the treatment of diseases such as cancer.

IC ICM C12N015-12
ICS C07K014-705; C12N015-62; C07K016-00; C12N005-10; A61K035-12

CC 15-10 (Immunochemistry)
Section cross-reference(s): 3

IT Immunoglobulins
RL: PRP (Properties)
(G4; effector cell activation via chimeric receptors : **DNA** delivery process and therapeutic potential)

IT **Protein** motifs
(ITAM; of **chimeric** receptors in relation to effector cell

activation and immunotherapy)
IT Cell activation
(T cell; cellular **transfection** with chimeric receptors for effector function activation and therapy)
IT Lymphocyte
T cell (lymphocyte)
(activation; cellular **transfection** with chimeric receptors for effector function activation and therapy)
IT Suspensions
(agents; for cellular **transfection** with chimeric receptors for effector function activation and therapy)
IT Synthetic gene
Synthetic gene
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(animal; for cellular **transfection** with chimeric receptors for effector function activation and therapy)
IT Macromolecular compounds
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biol.; cellular **transfection** with chimeric receptors for effector function activation and therapy)
IT Adoptive immunotherapy
Allergy inhibitors
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antitumor agents
B cell (lymphocyte)
Cell membrane
Dendritic cell
Genetic vectors
Macrophage
Monocyte
Plasmids
Signal transduction, biological
Virus vectors
(cellular **transfection** with chimeric receptors for effector function activation and therapy)
IT Cystic fibrosis
Dermatitis
Eczema
Infection
Psoriasis
Sickle cell anemia
Transplant rejection
(cellular **transfection** with chimeric receptors for effector function activation and therapy of)
IT Receptors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric; cellular **transfection** with chimeric receptors for effector function activation and therapy)
IT **DNA**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes, condensed, with protamines or polylysine; cellular

transfection with chimeric receptors for effector function activation and therapy)

IT Disease, animal
(congenital; cellular **transfection** with chimeric receptors for effector function activation and therapy of)

IT T cell (lymphocyte)
(cytotoxic; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Metabolism, animal
(disorder; cellular **transfection** with chimeric receptors for effector function activation and therapy of)

IT Lymphocyte
T cell (lymphocyte)
(effector cell; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Mucins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(episialins; cellular **transfection** with chimeric receptors for effector function activation against)

IT Dispersing agents
Human adenovirus
Stabilizing agents
(for cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT **Proteins**, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene B29; as cytoplasmic component for **chimeric** receptor mediating effector cell activation)

IT Transplant and Transplantation
(graft-vs.-host reaction; cellular **transfection** with chimeric receptors for effector function activation and therapy of)

IT Intestine, disease
(inflammatory; cellular **transfection** with chimeric receptors for effector function activation and therapy of)

IT Drug delivery systems
(liposomes; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Cell activation
(lymphocyte; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Lymphocyte
(natural killer cell; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Nerve, disease
(neuropathy; cellular **transfection** with chimeric receptors for effector function activation and therapy of)

IT **Signal peptides**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(of chimeric receptors in relation to effector cell activation and immunotherapy)

IT **DNA** sequences
Protein sequences
(of humanized **chimeric** receptors)

IT Drug delivery systems
(parenterals; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Hematopoietic precursor cell
(stem; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Gene, animal
Gene, animal
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthetic; for cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Multiple sclerosis
(therapeutic agents; cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-assocd.; cellular **transfection** with chimeric receptors for effector function activation against)

IT 193227-49-5 193227-51-9 193227-53-1 193227-55-3 193227-57-5
193227-59-7
RL: PRP (Properties)
(amino acid sequence; effector cell activation via chimeric receptors : **DNA** delivery process and therapeutic potential)

IT 25104-18-1D, Polylysine, **DNA** complexes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cellular **transfection** with chimeric receptors for effector function activation and therapy)

IT 193227-48-4 193227-50-8 193227-52-0 193227-54-2 193227-56-4
193227-58-6
RL: PRP (Properties)
(**nucleotide** sequence; effector cell activation via chimeric receptors : **DNA** delivery process and therapeutic potential)

L42 ANSWER 27 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:140281 HCAPLUS
DOCUMENT NUMBER: 126:140576
TITLE: Mammalian expression vector system for non-secretor genes
INVENTOR(S): Okasinski, Gregory F.; Schaefer, Verlyn G.; Suhar, Thomas S.; Lesniewski, Richard R.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9641179	A1	19961219	WO 1996-US9345	19960605
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6020122	A	20000201	US 1995-478073	19950607
CA 2223182	AA	19961219	CA 1996-2223182	19960605
EP 830602	A1	19980325	EP 1996-918273	19960605
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 11508035	T2	19990713	JP 1996-501685	19960605

PRIORITY APPLN. INFO.: US 1995-478073 19950607
WO 1996-US9345 19960605

AB A mammalian expression system is described capable of generating high levels of recombinant proteins from non-secretor genes. In particular, a plasmid is described for the expression of the hepatitis C virus (HCV) E2

antigen. Plasmid 577 is constructed as a cloning vehicle comprising (1) expression control regions, (b) a region coding for the rabbit Ig heavy chain .gamma. secretion signal sequence, (c) bacterial enzyme for selection in eukaryotic cells, (d) an amplification system suitable for enhanced expression in eukaryotic cells, and (e) the region coding for the protein of interest. The signal region includes the N-terminal Ser-Asp-Glu-Leu sequence of human pro-urokinase, which is intended to promote signal protease processing, efficient secretion, and final product stability in culture fluids. This expression system allows for the prodn. of high levels of HCV proteins, allowing the proper processing, glycosylation, and conformation (folding) of the viral protein(s) in the system, and the HCV E2 fusion protein can be recovered extracellularly as well as intracellularly. Plasmid 577 contg. the HCV E2 antigen fusion protein is transfected in dihydrofolate reductase-deficient CHO cells and yields recombinant E2 antigen able to function in antibody assays. Also provided are several immunoassays which utilizes the fusion protein, a test kit which contains the fusion protein, a diagnostic reagent which comprises the fusion protein, and a vaccine which utilizes the fusion protein produced by the disclosed plasmid.

IC ICM G01N033-543
ICS G01N033-576; G01N033-569; C12N015-11; A61K039-12

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 9, 15, 63

ST mammalian expression plasmid vector nonsecretory protein; **transfection** mammalian expression plasmid vector; hepatitis C **virus** E2 antigen cloning; immunoassay HCV E2 antigen cloning

IT Hepatitis C **virus**
(E2 antigen **fusion protein** prodn. for antibody immunoassays; mammalian expression vector system for non-secretor genes)

IT Antigens
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(E2, hepatitis C **virus**, fusion product with IgG .gamma.-chain **signal peptide**; mammalian expression vector system for non-secretor genes)

IT Immunoglobulins
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G, .gamma.-chain, fusion product with hepatitis C **virus** E2 antigen; mammalian expression vector system for non-secretor genes)

IT **Fusion proteins (chimeric proteins)**
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(IgG .gamma.-chain signal sequence fused with nonsecretory **proteins**; mammalian expression vector system for non-secretor genes)

IT **Signal peptides**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusion products; mammalian expression vector system for non-secretor genes)

IT Immunoglobulins
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(heavy chains, .gamma., fusion product with hepatitis C **virus** E2 antigen; mammalian expression vector system for non-secretor genes)

IT Immunoassay
(hepatitis C **virus** E2 antigen **fusion** **protein** prodn. for antibody immunoassays; mammalian expression vector system for non-secretor genes)

IT Antibodies
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hepatitis C **virus** E2 antigen **fusion** **protein** prodn. for antibody immunoassays; mammalian expression vector system for non-secretor genes)

IT Vaccines
(hepatitis C **virus** E2 antigen **fusion** **protein** prodn. for vaccines; mammalian expression vector system for non-secretor genes)

IT 186618-90-6P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**nucleotide** sequence; mammalian expression vector system for non-secretor genes)

L42 ANSWER 28 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:541974 HCAPLUS
DOCUMENT NUMBER: 125:218523
TITLE: Molecular cloning of a novel T cell-directed CC chemokine expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector
AUTHOR(S): Imai, Toshio; Yoshida, Tetsuya; Baba, Masataka; Nishimura, Miyuki; Kakizaki, Mayumi; Yoshie, Osamu
CORPORATE SOURCE: Shionogi Inst. for Medical Science, Osaka, 566, Japan
SOURCE: Journal of Biological Chemistry (1996), 271(35), 21514-21521
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Precursors of most secreted and cell surface mols. carry signal sequences at their amino termini. Here the authors describe an efficient **signal** sequence **trap** method and isolation of a novel CC chemokine. An expression library was constructed by inserting 5' portion-enriched cDNAs from phytohemagglutinin-stimulated peripheral blood mononuclear cells into upstream of signal sequence-deleted CD4 cDNA in an Epstein-Barr virus shuttle vector. After electroporation into Raji cells, CD4 antigen-pos. cells were enriched by repeated cell sorting and plasmids were recovered in Escherichia coli. Out of 100 plasmid clones examd., 42 clones directed expression of CD4 antigen on the cell surface. Among them were signal sequences of CD6, .beta.2-microglobulin, MGC-24, and T cell receptor .epsilon.-chain, and at least four novel potential signal sequences. A cDNA clone encoding a novel CC chemokine was isolated by using one of the trapped fragments. The gene designated as TARC from Thymus and Activation-Regulated Chemokine was expressed transiently in phytohemagglutinin-stimulated peripheral blood mononuclear cells and constitutively in thymus. Radiolabeled recombinant TARC specifically bound to T cell lines and peripheral T cells but not to monocytes or granulocytes. The binding of radiolabeled TARC to the high-affinity receptor (Kd, 2.1 nM) on Jurkat was displaced by TARC but not by

interleukin-8, MIP-1.alpha., RANTES, or MCP-1. TARC also bound to the promiscuous chemokine receptor on erythrocytes (Kd, 17 nM). TARC induced chemotaxis in T cell lines Hut78 and Hut102. Pretreatment of Hut78 with pertussis toxin abolished the TARC-induced cell migration. Collectively, T cells express a highly selective receptor for TARC that is coupled to pertussis toxin-sensitive G-protein. TARC may BE a factor playing important roles in T cell development in thymus as well as in trafficking and activation of mature T cells.

CC 14-3 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3

ST chemokine TARC sequence T cell chemotaxis; **signal** sequence **trap** Epstein Barr **virus**

IT Chemotaxis
(T cell; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(expression; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Combinatorial library
Molecular cloning
Protein sequences
Thymus gland
Transcription, genetic
(mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Erythrocyte
(promiscuous chemokine receptor of; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Genetic methods
(**signal** sequence **trap**; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Antigens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CD4, **signal** sequence-deleted; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT **Virus**, animal
(Epstein-Barr, mol. cloning of human T cell-directed CC chemokine TARC

expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Lymphocyte
(T-cell, mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Lymphokine and cytokine receptors
Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chemokine, TARC; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Lymphokine and cytokine receptors
Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chemokine, promiscuous, of erythrocytes; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Deoxyribonucleic acid sequences
(complementary, mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT Leukocyte
(mononuclear, mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT 181532-29-6
RL: PRP (Properties)
(amino acid sequence; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

IT 181011-50-7, GenBank D43767
RL: PRP (Properties)
(nucleotide sequence; mol. cloning of human T cell-directed CC chemokine TARC expressed in thymus by **signal** sequence **trap** using Epstein-Barr **virus** vector and pertussis toxin-sensitive G-protein-coupled T cell receptor)

L42 ANSWER 29 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:342220 HCAPLUS
DOCUMENT NUMBER: 125:2984
TITLE: Modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs
INVENTOR(S): Curiel, David T.; Deshane, Jessy
PATENT ASSIGNEE(S): Uab Research Foundation, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9607321	A1	19960314	WO 1995-US10740	19950823
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5910486	A	19990608	US 1995-468252	19950606
PRIORITY APPLN. INFO.:			US 1994-301339	19940906
			US 1995-468252	19950606

AB Methods and compns. for modulating protein function in a cell involving intracellular expression of an antibody homolog that binds to the protein within the cell are disclosed. An antibody homolog, such as a single chain Fv (sFv) fragment, is expressed within an intracellular compartment of a cell, such as the endoplasmic reticulum (ER), to inhibit cell surface expression of a membrane protein. Preferably, the cell is a malignant mammalian cell and the protein is a cell surface receptor oncoprotein, such as c-erbB2. Intracellular binding of the antibody homolog to the receptor oncoprotein inhibits its surface expression and, moreover, inhibits cell proliferation and cell survival. Isolated nucleic acid mols. encoding anti-c-erbB2 antibody homologs, as well as recombinant expression vectors and host cells incorporating these nucleic acid mols., are also provided. Thus, a signal sequence directing expression to the endoplasmic reticulum (MKSHSQVFVFLLLCVSGAHG) was linked to the nucleotide sequence encoding anti-human erbB2 single-chain Fv antibody by PCR methods and cloned into the KpnI/XbaI sites of pCDNA3 to forma construct named pGT21. Transient transfection of the plasmid vector in the human ovarian carcinoma cell line SKOV3 was achieved by the adenovirus-polylysine method. Expression intracellularly of the endoplasmic reticulum-expressed form of anti-erbB2 sFv in erbB2 over-expressing carcinoma cells (the ovarian carcinoma cell line SKOV3) results in decreased cell surface expression of erbB2, decreased cellular proliferation, decreased cell survival, and decreased tumorigenicity.

IC ICM A01N043-04

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 15

ST carcinoma erbB2 oncoprotein regulation antibody **transfection**

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human gene c-erbB2 receptor, fusion product with endoplasmic reticulum-directing **signal peptide**; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT Plasmid and Episome
Virus, animal
(expression vector; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene c-erbB2, antibody to, fusion products with endoplasmic reticulum-directing **signal peptide**; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p185c-erbB2, antibody to, fusion products with endoplasmic

reticulum-directing **signal peptide**; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT **Peptides**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**signal**, endoplasmic reticulum-directing, fusion products with anti-gene c-erbB2 receptor antibody; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transforming, antibody to, **fusion** products with endoplasmic reticulum-directing signal sequence; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT 177413-77-3
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(endoplasmic reticulum-directing **signal peptide**; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT 177474-95-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nucleotide** sequence; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

IT 177474-94-1
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nucleotide** sequence; modulating oncoprotein c-erbB2 function in carcinoma cells using intracellularly-expressed antibody homologs)

L42 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:887967 HCAPLUS
DOCUMENT NUMBER: 123:278075
TITLE: Retroviral vector particles for transducing non-proliferating cells with integration of the transforming **nucleic acid**
INVENTOR(S): Mason, James M.; Kennedy, Scott P.
PATENT ASSIGNEE(S): Alexion Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9519428	A1	19950720	WO 1995-US453	19950112
W: JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5576201	A	19961119	US 1994-182612	19940114

PRIORITY APPLN. INFO.: US 1994-182612 19940114
AB Retroviral vector particles for the introduction of transforming DNA into a target cell are produced in cells carrying a packaging plasmid vector

carrying the gag, pol, and env genes of an oncogenic retrovirus. The gag gene of the plasmid is modified to incorporate a nuclear localization signal and the plasmid also carries the foreign DNA for delivery. These particles can be used to transfect non-proliferating cells, including stem cells and neurons. The presence of the NLS sequence allows at least one on of these genes to enter the nucleus of a target cell, thus allowing integration of the gene into the genome of the target cell. Specifically, the gag protein of Moloney murine leukemia virus has the NLS peptide of SV40 large T antigen incorporated into it.

IC ICM C12N007-00
ICS C12N015-00; C12N015-11; C12N015-48; C12N015-86; C07K014-00; C07K014-15

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 10

IT **Peptides**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(NLS (nuclear localization **signal**), gag proteins contg.; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT **Deoxyribonucleic** acid sequences
(of gag gene and derivs. of Moloney murine leukemia **virus**; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Protein sequences
(of gag protein and derivs. of Moloney murine leukemia **virus**; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Plasmid and Episome
(pMA/NLS, MMuLV **virus** gag gene carrying SV40 nuclear localization sequence on; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Transformation, genetic
(retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Nerve
(**transfection** of; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT **Virus**, animal
(Moloney murine leukemia, gag gene of, NLS-encoding sequence in; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(env, retroviral transformation vectors contg.; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gag, retroviral transformation vectors contg., nuclear localization signal in; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(gene gag, **fusion** products with nuclear localization peptides; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**
)

IT Antigens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(large T, nuclear localization signal of, in gag proteins; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(pol, retroviral transformation vectors contg.; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT **Virus**, animal
(retro-, for delivery of transforming **nucleic acids**
; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT **Virus**, animal
(simian 40, NLS of, in integrating retroviral vectors; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT Cell
(stem, **transfection** of; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT 169551-85-3D, **fusion** products with gag **proteins**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence, SV40 T antigen nuclear location sequence; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT 95088-49-6D, **fusion** products with gag **proteins**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence, SV40 large T antigen nuclear location sequence; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT 169665-39-8P 169665-40-1P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT 169665-37-6D, fusion products with nuclear localization peptides
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

IT 169665-38-7 169665-41-2 169665-42-3
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(**nucleotide** sequence; retroviral vector particles for transducing non-proliferating cells with integration of transforming **nucleic acid**)

L42 ANSWER 31 OF 33 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:544549 HCAPLUS
DOCUMENT NUMBER: 117:144549
TITLE: Insecticidal effects of an insect-specific neurotoxin expressed by a recombinant baculovirus
AUTHOR(S): Maeda, Susumu; Volrath, Sandra L.; Hanzlik, Terry N.; Harper, S. Andrew; Majima, Kei; Maddox, Daryl W.; Hammock, Bruce D.; Fowler, Elizabeth
CORPORATE SOURCE: Dep. Entomol., Univ. California, Davis, CA, 95616, USA
SOURCE: Virology (1991), 184(2), 777-80
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The scorpion Androctonus australis has a peptide (AaIT) which selectively targets the insect sodium channel. This mode of action is similar to that of many widely used chem. insecticides. When Bombyx mori larvae were infected with a recombinant baculovirus carrying a synthetic AaIT gene, the expressed protein was secreted into the hemolymph and caused symptoms consistent with sodium channel blocking, including tremors and feeding cessation at 40 h p.i. followed by paralysis and death by 60 h p.i. Larvae infected with control virus died by 96 h p.i. These results indicate that foreign genes can be used in recombinant baculoviruses to reduce insect feeding damage and increase the rate of insect kill.

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 5, 12

IT Gene, animal
RL: BIOL (Biological study)
(for Bombyx mori **signal peptide**-Androctonus australis neurotoxin **fusion protein**, expression in recombinant baculovirus of, insecticidal effect on silk worm larvae of)

IT **Deoxyribonucleic** acid sequences
(neurotoxin Aa IT-specifying, of Androctonus australis expressed by recombinant baculovirus, complete)

IT Biological transport
(of Androctonus australis synthetic recombinant neurotoxin, by Baculovirus-**transfected** Bombyx mori larvae, Bombyx mori **signal peptide** in)

IT Silkworm
(**signal peptide** of, Androctonus australis neurotoxin **fusion** with, recombinant **protein** secretion and insecticidal activity in relation to)

IT **Peptides**, biological studies
RL: BIOL (Biological study)
(**signal**, Bombyx mori, in synthetic Androctonus australis neurotoxin secretion)

IT **Virus**, animal
(silkworm nuclear polyhedrosis, Androctonus australis synthetic neurotoxin gene cloned in, expression and secretion in Bombyx mori larvae of, insecticidal activity in relation to)

IT 143637-65-4 143637-66-5
RL: PRP (Properties); BIOL (Biological study)
(**nucleotide** sequence of)

L42 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:19422 HCAPLUS
DOCUMENT NUMBER: 110:19422
TITLE: Plasminogen activators, **DNA** encoding the same, and their preparation and use
INVENTOR(S): Devlin, James Joseph; Devlin, Patricia Egan; Mark, David Fu Chi; Clark, Robin
PATENT ASSIGNEE(S): Cetus Corp., USA

SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 273774	A2	19880706	EP 1987-311532	19871230
EP 273774	A3	19881214		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
WO 8805081	A2	19880714	WO 1987-US3362	19871217
WO 8805081	A3	19881020		
W: JP				
AU 8783093	A1	19880811	AU 1987-83093	19871229

PRIORITY APPLN. INFO.: US 1986-947846 19861230
US 1987-77586 19870724

AB Genes encoding protease-resistant urokinase muteins and recombinant plasminogen activators comprising a fibrin interaction domain and the protease domain of urokinase are constructed, plasmids for expression of these genes in microbial, animal, and insect cells are prepd., and the proteins are produced with transformants contg. these plasmids. COS cell expression plasmid pLP15, encoding a hybrid plasminogen activator comprising kringle-2 of tissue-type plasminogen activator, a linker, and the pro-urokinase protease domain, was constructed. The protease activity of this hybrid was stimulated .apprx.3.7-fold by fibrin while urokinase was stimulated only .apprx.1.7-fold.

IC ICM C12N015-00
ICS C12N009-72; C12N005-00; C12P021-02; A61K037-54
CC 3-4 (Biochemical Genetics)
IT **Virus**, animal
(baculo-, recombinant, insect cells infected with, hybrid plasminogen activators manuf. with)
IT Plasmid and Episome
(pPD18, **signal peptide**-hybrid plaminogen activator **fusion protein**-encoding gene on, for prepn. of recombinant baculovirus expression vectors)
IT **Peptides**, compounds
RL: BIOL (Biological study)
(**signal**, fusion products, with hybrid plasminogen activator, secretion from recombinant insect cells of)
IT 118057-86-6
RL: PRP (Properties)
(expression and **nucleotide** sequence of)
IT 9039-53-6, Urokinase
RL: PRP (Properties)
(**protease** domain of, recombinant plasminogen activators contg.)
IT 105913-11-9, Plasminogen activator
RL: PRP (Properties)
(recombinant, hybrid, urokinase **protease** domain and heterologous fibrin-binding domain in)
IT 118103-39-2
RL: PRP (Properties)
(**signal peptide**-encoding **DNA**, for secretion of hybrid recombinant plasminogen activators from insect cells)

L42 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1986:438263 HCAPLUS
DOCUMENT NUMBER: 105:38263
TITLE: DNA alterations photosensitized by tetracycline and some of its derivatives
AUTHOR(S): Piette, Jacques; Decuyper, Jean; Van de Vorst, Albert
CORPORATE SOURCE: Lab. Exp. Phys., Univ. Liege, Liege, Belg.
SOURCE: Journal of Investigative Dermatology (1986), 86(6), 653-8
CODEN: JIDEAE; ISSN: 0022-202X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Phage M13 mp10 DNA was irradiated with near-UV light in the presence of tetracycline derivs. and primed with synthetic oligonucleotide to be used for DNA synthesis using Escherichia coli DNA polymerase. Chain terminations were obsd. by denaturing PAGE and mapped precisely. All the synthesis stops occurred before or at the level of guanine residues, showing that the photoreaction mediated by tetracycline derivs. led to a preferential alteration of guanine residues. These lesions were demonstrated to be induced in DNA through a pathway involving singlet O. Tetracycline derivs. also photoinduced the breakage of the DNA sugar-phosphate backbone monitored by the conversion of supercoiled .vphi.X174 DNA to a relaxed form. This lesion was shown to be initiated by OH radicals. The prodn. of this free radical has been confirmed by ESR spin trapping expts. using 5,5-dimethyl-1-pyrroline-N-oxide as spin trap. In addn. to the EPR signal due to OH radicals, **trapping** another unassigned **signal** has been detected.

CC 8-3 (Radiation Biochemistry)
IT **Virus**, bacterial
(M13mp10, DNA of, photosensitization of, by tetracycline and derivs.)

```
=> fil wpids
FILE 'WPIDS' ENTERED AT 14:12:29 ON 06 FEB 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE LAST UPDATED:          4 FEB 2003      <20030204/UP>
MOST RECENT DERWENT UPDATE:     200308        <200308/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> DUE TO TECHNICAL ISSUES THE SDIS FOR UPDATES 200302-200304
    BASED ON ENTRY DATE (ED) MAY CONTAIN DOCUMENTS PREVIOUSLY
    DISTRIBUTED. IF YOU ENCOUNTER ANY SURPLUS DOCUMENTS OF THIS
    KIND, PLEASE CONTACT OUR HELPDESKS. UNJUSTIFIED CHARGES
    INCURRED WILL BE REVOKED OF COURSE.
    WE APOLOGIZE FOR ANY INCONVENIENCE CAUSED. <<<


>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d his

     (FILE 'WPIDS' ENTERED AT 13:49:03 ON 06 FEB 2003)
               DEL HIS Y
L1         34089 S VIRUS?
L2           208 S SINDBIS OR ALPHAVIRUS? OR ALPHA VIRUS?
L3           414 S VIRAL (3A) GENOME?
L4           619 S L2 OR L3
L5         76926 S NUCLEIC ACID? OR DNA OR ?NUCLEOTIDE?
L6           498 S L5 AND L4
L7           569 S SIGNAL (3A) TRAP?
L8             0 S L6 AND L7
L9             1 S L7 AND L1
L10         6596 S TRANSFECT?
L11          100 S L6 AND L10
L12        40826 S CHIMER? OR FUSION
L13           31 S L11 AND L12
L14         1166 S SIGNAL(3A) PEPTIDE?
L15           12 S L14 AND L6
L16          860 S SUPPRESS? (3A) CONDIT?
L17            1 S L6 AND L16
L18        13011 S LIBRAR?
L19           40 S L6 AND L18
L20           19 S L19 AND (L12 OR L10)
L21        12041 S PROTEAS?
L22           24 S L21 AND L6
L23           12 S L22 AND (L12 OR L10)
L24           22 S L9 OR L15 OR L17 OR L23
L25           76 S L1 AND (L7 OR L14) AND L12
L26            0 S CERULERIN
```

```
L27           38 S CERULENIN
L28           83 S L27 OR OKADAIC ACID#
L29            2 S L1 AND ( L27 OR L28)
L30           13 S FETTER
L31            1 S L30 AND  L1
L32            8 S L25 AND L21
L33            6 S L25 AND (C DNA OR CDNA) (4A) LIBRAR?
L34           35 S L33 OR L32 OR L31 OR L29 OR  L24

     FILE 'WPIDS' ENTERED AT 14:12:29 ON 06 FEB 2003

=> d que l34
L1         34089 SEA FILE=WPIDS ABB=ON  PLU=ON  VIRUS?
L2           208 SEA FILE=WPIDS ABB=ON  PLU=ON  SINDBIS OR ALPHAVIRUS? OR ALPHA
                 VIRUS?
L3           414 SEA FILE=WPIDS ABB=ON  PLU=ON  VIRAL (3A) GENOME?
L4           619 SEA FILE=WPIDS ABB=ON  PLU=ON  L2 OR L3
L5         76926 SEA FILE=WPIDS ABB=ON  PLU=ON  NUCLEIC ACID? OR DNA OR
                 ?NUCLEOTIDE?
L6           498 SEA FILE=WPIDS ABB=ON  PLU=ON  L5 AND L4
L7           569 SEA FILE=WPIDS ABB=ON  PLU=ON  SIGNAL (3A) TRAP?
L9             1 SEA FILE=WPIDS ABB=ON  PLU=ON  L7 AND L1
L10         6596 SEA FILE=WPIDS ABB=ON  PLU=ON  TRANSFECT?
L12        40826 SEA FILE=WPIDS ABB=ON  PLU=ON  CHIMER? OR FUSION
L14         1166 SEA FILE=WPIDS ABB=ON  PLU=ON  SIGNAL(3A) PEPTIDE?
L15           12 SEA FILE=WPIDS ABB=ON  PLU=ON  L14 AND L6
L16          860 SEA FILE=WPIDS ABB=ON  PLU=ON  SUPPRESS? (3A) CONDIT?
L17            1 SEA FILE=WPIDS ABB=ON  PLU=ON  L6 AND L16
L21        12041 SEA FILE=WPIDS ABB=ON  PLU=ON  PROTEAS?
L22           24 SEA FILE=WPIDS ABB=ON  PLU=ON  L21 AND L6
L23           12 SEA FILE=WPIDS ABB=ON  PLU=ON  L22 AND (L12 OR L10)
L24           22 SEA FILE=WPIDS ABB=ON  PLU=ON  L9 OR L15 OR L17 OR L23
L25           76 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 AND (L7 OR L14) AND L12
L27           38 SEA FILE=WPIDS ABB=ON  PLU=ON  CERULENIN
L28           83 SEA FILE=WPIDS ABB=ON  PLU=ON  L27 OR OKADAIC ACID#
L29            2 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 AND ( L27 OR L28)
L30           13 SEA FILE=WPIDS ABB=ON  PLU=ON  FETTER
L31            1 SEA FILE=WPIDS ABB=ON  PLU=ON  L30 AND  L1
L32            8 SEA FILE=WPIDS ABB=ON  PLU=ON  L25 AND L21
L33            6 SEA FILE=WPIDS ABB=ON  PLU=ON  L25 AND (C DNA OR CDNA) (4A)
                 LIBRAR?
L34           35 SEA FILE=WPIDS ABB=ON  PLU=ON  L33 OR L32 OR L31 OR L29 OR
                 L24


=> d .wp 1-34

L34  ANSWER 1 OF 35  WPIDS (C) 2003 THOMSON DERWENT
AN   2002-529488 [57]    WPIDS
DNN  N2002-419367        DNC C2002-149854
TI   Novel attenuated bovine viral diarrhea virus that carries a mutated
     protease coding sequence and a bovine ubiquitin coding sequence in
     its viral genome, useful for treating infection caused
     by the virus in an animal.
DC   B04 C06 D16 S03
IN   CAO, X; ZYBARTH, G M
PA   (PFIZ) PFIZER PROD INC
CYC  1
PI   CA 2363493     A1 20020522 (200257)* EN   56p
ADT  CA 2363493 A1 CA 2001-2363493 20011120
```

PRAI US 2000-256515P 20001218; US 2000-252513P 20001122
AB CA 2363493 A UPAB: 20020906
NOVELTY - An attenuated bovine viral diarrhea (BVD) virus (I), that carries in its **viral genome** a mutated Npro coding sequence comprising an intact 5' region, and a sequence coding for a monomeric bovine ubiquitin, where the ubiquitin coding sequence is operably placed between the 3' end of the mutated Npro coding sequence and the 5' end of the coding sequence for the viral core protein, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated **nucleic acid** molecule (II) comprising the genomic sequence of (I);

(2) a vector (III) comprising (II) with a sequence (S1) of 12611 base pairs fully defined in the specification or its degenerate variant;

(3) a cell (IV) transformed or **transfected** with (II);

(4) modifying (M1) the genomic **nucleic acid** molecule of an isolated wild type BVD virus, by introducing a mutation into the 3' region of the Npro **protease** gene, where the mutation renders the Npro protein inactive, and inserting a sequence coding for a monomeric bovine ubiquitin between the mutated Npro coding sequence and the coding sequence of the core protein;

(5) attenuating (M2) an isolated wild type BVD virus, by isolating the genomic **nucleic acid** molecule from the virus, introducing a mutation into the 3' region of the Npro **protease** gene in the **viral genome**, where the mutation renders the Npro protein inactive, inserting a sequence coding for a monomeric bovine ubiquitin between the mutated Npro coding sequence and the coding sequence of the core protein, and producing from the modified genome an attenuated virus suitable for use in a vaccine;

(6) an immunogenic composition (V) comprising (I) or (II) and a veterinarily-acceptable carrier;

(7) a vaccine composition (VI) comprising (II) and a veterinarily-acceptable carrier;

(8) identifying (M3) a BVD virus in an animal as (I), where the animal is suspected of suffering from a BVD virus (BVDV) infection, by isolating the virus from the animal, and detecting the presence of the ubiquitin coding sequence, therefore determining the isolated virus as identical to (I); and

(9) a kit (VII) comprising (V) or (VI), and instructions for use of (V) for inducing an immune response against BVDV in an animal subject or for using (VI) as a vaccine for preventing or treating a BVDV infection in an animal.

ACTIVITY - Virucide.

MECHANISM OF ACTION - Vaccine.

No suitable data given.

USE - (I) is useful for inducing an immune response against BVDV in an animal subject, for treating a BVDV infection in an animal, or in the preparation of a medicament for inducing an immune response against BVDV in an animal subject or for treating a BVDV infection in an animal (claimed). (I) or (II) is useful for raising antibodies against BVDV or in vaccines designed to protect cattle from viral infection.

ADVANTAGE - (I) replicates faster than BVDdN1, provides higher immunogenicity for protection, and permits large-scale production of more effective vaccines against BVDV infections.

Dwg.0/4

TECH UPTX: 20020906
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Virus: (I) comprises (S1) or its degenerate variant.
Preferred Vector: (III) is designated as pBVDdN6 (ATCC No. PTA-2532) comprising a sequence of 16758 base pairs fully defined in the

specification.

L34 ANSWER 2 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-471503 [50] WPIDS
DNN N2002-372200 DNC C2002-134104
TI Isolating and characterizing an expression regulatory sequence for expressing recombinant polypeptides and/or RNA, comprises producing oligonucleotide primers that amplify sequences upstream or downstream of cDNAs.
DC C06 D16 P13
IN ARCAND, F; BILODEAU, P; D'AOUST, M; VEZINA, L
PA (MEDI-N) MEDICAGO INC
CYC 98
PI WO 2002036786 A2 20020510 (200250)* EN 74p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002010310 A 20020515 (200258)
ADT WO 2002036786 A2 WO 2001-CA1532 20011031; AU 2002010310 A AU 2002-10310 20011031
FDT AU 2002010310 A Based on WO 200236786
PRAI US 2000-244214P 20001031
AB WO 200236786 A UPAB: 20020807
NOVELTY - Isolating and characterizing (M1 and 2) an expression regulatory sequence for the expression of recombinant polypeptides and/or RNA comprising producing at least one oligonucleotide primer from **cDNAs** of a **cDNA library**, where the oligonucleotide primer allows amplification of genomic sequences upstream or downstream of the cDNAs, is new.

DETAILED DESCRIPTION - Isolating and characterizing (M1 and 2) an expression regulatory sequence for the expression of recombinant polypeptides and/or RNA comprising producing at least one oligonucleotide primer from **cDNAs** of a **cDNA library**, where the oligonucleotide primer allows amplification of genomic sequences upstream or downstream of the cDNAs. Where, (M1) comprises:

(a) isolating mRNA from a cell;

(b) preparing a **cDNA library** from the mRNA;

(c) producing at least one oligonucleotide primer from **cDNAs** of the **cDNA library** which allows amplification of genomic sequences upstream or downstream of the cDNAs;

(d) amplifying the genomic sequences upstream or downstream of the cDNAs with the oligonucleotide primer on a genomic sample;

(e) linking the amplified sequence to a gene encoding for a detectable polypeptide and/or RNA to form a DNA expression vector for expression of the detectable, polypeptide and/or RNA; and

(f) selecting an expression regulatory sequence of a vector by measuring the level of expression of the detectable polypeptide and/or RNA under conditions allowing activation of the expression regulatory sequence and expression of the detectable polypeptide and/or RNA; and

(M2) comprises:

(a) producing at least one oligonucleotide primer from a cDNA, genomic DNA fragment or synthetic DNA sequence which allows amplification of a genomic sequence upstream or downstream of a genomic complementary site of the oligonucleotide primer in a genomic DNA sample;

(b) amplifying the genomic sequence upstream or downstream of the genomic complementary site of the oligonucleotide primer on a genomic DNA sample;

(c) linking an amplified sequence obtained from (b) to a gene encoding for a detectable polypeptide and/or RNA to form a DNA expression vector for expressing the detectable polypeptide and/or RNA; and

(d) selecting at least one expression regulatory sequence from the vector of (b) by measuring levels of expression of the detectable polypeptide and/or RNA under a condition allowing activation of the expression regulatory sequence and expression of the detectable polypeptide and/or RNA.

INDEPENDENT CLAIMS are included for the following:

(1) producing (M3) adapted DNA expression vector for expression of recombinant polypeptides and/or RNA by employing the method of M1 or M2;

(2) a transgenic plant (I) regenerated from stably genetically transformed cell;

(3) a plant cell (II) transformed with the DNA expression vector above;

(4) a transgenic plant (III) regenerated from the plant cell of (4); and

(5) producing (M4) recombinant polypeptides and/or RNA using a plant cell and/or the transgenic plant above.

USE - (M1) and (M2) are useful for isolating, characterizing and identifying a large number of known and unknown promoters that are active under any desired environmental condition to which a cell may be exposed, and not just to the exemplified isolation of promoters that are capable of expression in specific conditions. The methods are also useful for cloning genes from any host, or from a specific tissue with such host, from which a **cDNA library** may be constructed; for the identification and isolation of analogous promoters, **signal peptides**, and structural genes in several species of multicellular and unicellular organisms, and as a high throughput identification system of candidate therapeutic targets. The promoter sequences may be used to regulate the synthesis of polypeptides.

Dwg.0/5

TECH UPTX: 20020807

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The cell is a plant cell, preferably an alfalfa cell. The gene encoding polypeptide and/or RNA is from an animal, a mammal, a plant, an insect, a yeast, a mold, a bacterium, or a **virus**. The polypeptide and/or RNA is selected from a pharmaceutical, an agronomical, an environmental, an industrial, a nutriceutical, a cosmeceutical, a polypeptide, a gene product marker, a **fusion** protein, a green fluorescent protein, and a beta-glucuronidase. The condition allowing the activation of the expression regulatory sequence and of the detectable polypeptide and/or RNA is an in vitro or in vivo condition, where in vitro conditions allow the expression of detectable polypeptide and/or RNA from a transitory transfected cell, a stably genetically transformed cell, or in a reaction buffer. The in vivo expression is expression in a cultured cell, or in a growing organism. The polypeptide and/or RNA comprises a tag to be directly detected or for purification of the polypeptide, and is indirectly detected by using antibodies, Western blot, Northern blot, in situ hybridization, colorimetry, optical densitometry, spectrophotometry, or electrophoresis. The tag is a self-cleavable tag. The genomic sequences comprise expression regulatory sequence which is further sequenced, natively located upstream or downstream of a gene encoding a polypeptide and/or RNA, and controls the expression of the gene encoding a polypeptide and/or RNA. The DNA expression vector comprising the genomic sequence comprises an expression regulatory sequence. The DNA expression vector is a plasmid vector or a viral vector.

L34 ANSWER 3 OF 35 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-426956 [45] WPIDS

DNC C2002-121140
TI Analyzing phenotype of human immune deficiency virus, useful for optimizing therapy, by cloning segment into viral particle and **transfecting** cell containing inducible marker gene.
DC B04 D16
IN CLAVEL, F; DAM, E; MAMMANO, F; OBRY, V; RACE, E; TROUPLIN, V
PA (BIOA-N) BIOALLIANCE PHARMA; (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (BIOA-N) BIOALLIANCE PHARMA SA; (CLAV-I) CLAVEL F; (DAME-I) DAM E; (MAMM-I) MAMMANO F; (OBRY-I) OBRY V; (RACE-I) RACE E; (TROU-I) TROUPLIN V
CYC 98
PI WO 2002038792 A2 20020516 (200245)* FR 98p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2816634 A1 20020517 (200245)
FR 2816635 A1 20020517 (200245)
AU 2002023052 A 20020521 (200260)
US 2002123036 A1 20020905 (200260)
ADT WO 2002038792 A2 WO 2001-FR3512 20011109; FR 2816634 A1 FR 2000-14495 20001110; FR 2816635 A1 FR 2001-3970 20010323; AU 2002023052 A AU 2002-23052 20011109; US 2002123036 A1 US 2001-817135 20010327
FDT AU 2002023052 A Based on WO 200238792
PRAI US 2001-817135 20010327; FR 2000-14495 20001110; FR 2001-3970 20010323
AB WO 200238792 A UPAB: 20020717
NOVELTY - Analyzing phenotype of HIV (human immune deficiency virus), resulting from one or more mutations in the **viral genome** that influence infection, in a patient sample, is new.

DETAILED DESCRIPTION - Analyzing phenotype of HIV (human immune deficiency virus), resulting from one or more mutations in the **viral genome** that influence infection, in a patient sample, is new. **Nucleic acids** are extracted from the sample, segments of them amplified by PCR (polymerase chain reaction) using pairs of primers that flank a genomic sequence susceptible to mutation, and a first host cell (HC1) **transfected** with:

(a) the amplicon;

(b) a vector containing parts of the HIV genome required for replication, except for the amplified segment and optionally also the env gene; and

(c) if the vector of (b) lacks the env gene, also a second vector containing this gene.

Homologous recombination occurs to produce a **chimeric** virus and HC1 are cultured to produce viral particles (VP) during a single cycle of replication. VP are used to infect at least one second host cell (HC2) that contains a marker gene (MG) that is activated only after viral infection, then the expressed marker detected and/or quantified to detect at least one characteristic of the original HIV.

An INDEPENDENT CLAIM is also included for a kit for performing the new process.

USE - The method is used to characterize HIV for optimization of treatment.

ADVANTAGE - The method allows rapid testing (7 days, making it suitable for routine use) of phenotypic characteristics associated with infectivity, replicative capacity and virulence, susceptibility/resistance to antiretroviral agents or natural antibodies, and tropism for particular co-receptors. The method requires only a single round of replication, reducing the risk that mutations will be lost.

Dwg.0/6
TECH UPTX: 20020717
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Process: Amplification uses primers that flank all or part of the gag, pol, **protease**, reverse transcriptase (RT), RNase H, integrase, vif, vpr, tat, rev, vpu, env, nef, cis-active, long terminal repeat, dimerization, splice-regulating or rev-response sequences. The region containing part of gag and the **protease** gene is amplified and the vector used then lacks at least part of the **protease** gene. Especially, amplification for detecting at least one mutation in the **protease** gene comprises a first round with primers FitA and ProA and a second round with FitB and ProB 5'-TCACCTAGAACTTTAAATGC (FitA) 5'-GGCAAATACTGGAGTATTGTATG (ProA) 5'-AGAACTTTAAATGCATGGGT (FitB) 5'-GGAGTATTGTATGGATTTTCAGG (ProB) to produce an amplicon of 1488 base pairs (residues 1237-2725 of the **viral genome**) and this used with a vector that:
(a) has a deletion from the pol open reading frame from residues 1505-2565 (encoding **protease**); and
(b) includes a single MluI restriction site.
Primer pairs for amplification of other preferred regions in the RT, gag, **protease**, integrase and/or env gene are reproduced. HC2 may be treated, before or during infection with VP, with:
(a) an inhibitor of RT or integrase, of the **fusion** targeting the gp41 viral protein, or of viral entry;
(b) an inhibitory antibody; or
(c) an inhibitor that targets co-receptors, optionally at several concentrations, and the effects of these compounds on expression of MG measured to determine susceptibility of the HIV isolate to them. Particularly susceptibility to hydroxyurea is tested and in all cases HC2 are cultured for 12-72, preferably 24-48, hours To determine tropism of the HIV for cellular receptors, two different HC2 are infected with VP and MG expression compared, particularly where one HC2 expresses the CCR5 receptor and the other the CXCR4 receptor. To determine infective and replicative capacity of HIV, MG expression is compared between cells infected with VP and those infected with similar VP derived from a reference virus, especially from the same subject but at an earlier stage (or before) therapy.
Preferred Kits: The kits comprise primer pairs, vectors that lack the env gene and amplified segment, vector containing an env gene, HC1 and 2, reagents for performing PCR, and reagents for detecting MG expression.
Preferred Cells: HC1 are not permissive for HIV infection, e.g. HeLa or 293T cells.

L34 ANSWER 4 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-404555 [43] WPIDS
DNN N2002-317560 DNC C2002-113640
TI Moraxella polypeptide and **polynucleotides** useful as vaccine for immunizing a host e.g. humans against disease e.g. otitis media, pneumonia, caused by infection of the bacteria.
DC B04 D16 S03
IN BRADLEY, B; LOOSMORE, S; OCHS, M; WANG, J; YANG, Y
PA (AVET) AVENTIS PASTEUR LTD
CYC 97
PI WO 2002018595 A2 20020307 (200243)* EN 277p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001087430 A 20020313 (200249)
ADT WO 2002018595 A2 WO 2001-CA1221 20010828; AU 2001087430 A AU 2001-87430 20010828
FDT AU 2001087430 A Based on WO 200218595
PRAI US 2000-230252P 20000906; US 2000-228294P 20000828; US 2000-228295P 20000828; US 2000-228296P 20000828; US 2000-228438P 20000829; US 2000-228439P 20000829; US 2000-228440P 20000829; US 2000-228441P 20000829; US 2000-228442P 20000829; US 2000-228443P 20000829; US 2000-228511P 20000829; US 2000-228512P 20000829; US 2000-228742P 20000829; US 2000-228773P 20000829; US 2000-229465P 20000901; US 2000-229474P 20000901; US 2000-229475P 20000901; US 2000-229478P 20000901; US 2000-229740P 20000905; US 2000-229803P 20000905; US 2000-229804P 20000905; US 2000-229805P 20000905; US 2000-229806P 20000905; US 2000-229809P 20000905; US 2000-229811P 20000905; US 2000-230214P 20000906; US 2000-230250P 20000906
AB WO 200218595 A UPAB: 20020709
NOVELTY - A Moraxella polypeptide (I) comprises a fully defined sequence (S1) of 502, 109, 108, 136, 224, 256, 507, 469, 289, 356, 228, 450, 473, 165, 164, 387, 180, 189, 208, 609, 522, 276, 678, 516, 913, 814 or 344 amino acids as given in the specification; a fragment (F1) of 12 consecutive amino acids of (I), or a polypeptide 75% identical to (S1) or F1, is new.

DETAILED DESCRIPTION - A Moraxella polypeptide (I) with a fully defined sequence (S1) of 502, 109, 108, 136, 224, 256, 507, 469, 289, 356, 228, 450, 473, 165, 164, 387, 180, 189, 208, 609, 522, 276, 678, 516, 913, 814 or 344 amino acids as given in the specification; a fragment (F1) of 12 consecutive amino acids of (I) which elicits an immunogenic response in a mammal against a bacterium of the Moraxella genus, or a polypeptide 75% identical to S1 or F1 capable of eliciting the same immunogenic response.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated **polynucleotide** (II) comprising a sequence which encodes (I);

(2) a **polynucleotide** (III) having a sequence complementary to (II);

(3) a fusion protein (IV) comprising (I) and another polypeptide;

(4) a **polynucleotide** (V) encoding (IV);

(5) a host organism (VI) comprising (II) optionally comprising a second **polynucleotide** encoding and capable of expressing additional polypeptides;

(6) an **oligonucleotide** (OLI) of 5-100 (preferably 10-40) **nucleotides** which hybridizes under stringent conditions to a sequence (S2) of 1759, 530, 557, 611, 875, 971, 1724, 1610, 1074, 1285, 898, 1553, 1650, 700, 695, 1396, 743, 770, 827, 2049, 1769, 1041, 2237, 1741, 2942, 2646 or 1234 **nucleotides** as given in the specification, or to a complementary to antisense sequence of (S2);

(7) preparation of (I) or (IV);

(8) an antibody (Ab) against (I) or (IV);

(9) a pharmaceutical composition (C1) comprising (I)/(II) and a carrier;

(10) a pharmaceutical composition (C2) comprising Ab and a carrier or diluent; and

(11) a diagnostic kit comprising (I), (II), Ab, (IV) or OLI and instructions for use.

ACTIVITY - Antiinflammatory; auditory; antibacterial.

MECHANISM OF ACTION - Vaccine. No supporting data is given.

USE - (I), (II), Ab, (IV) or OLI (primer or probe) is useful for detecting or diagnosing Moraxella infection by contacting the body fluid of the mammal to be tested with one of the above components. (I), (II) or (IV) is useful for generating antibodies specific for Moraxella (claimed), where the disorders of the infection include otitis media, respiratory

infection, sinusitus, and pneumonia. (I) or (II) is useful as a vaccine for immunizing against Moraxella infection.
Dwg.0/59

TECH UPTX: 20020709
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) or (IV) is prepared by culturing (VI) (claimed).
Preferred Fusion Protein: The second polypeptide of (IV) is preferably a heterologous **signal peptide** and has adjuvant activity.
Preferred **Polynucleotide**: (II), (III) or (V) is operatively linked to one or more expression control sequences.
Preferred Host Cell: In (VI), the additional **polynucleotide** encodes a polypeptide which is a Moraxella polypeptide, and (VI) is preferably a virus which is adeno virus, **alpha virus** or poxvirus especially vaccinia or canary pox virus, or a bacterium which is from Escherichia coli, Shigella, Salmonella, Vibrio cholerae, Lactobacillus, Streptococcus, Bacille Calmette-Guerin (BCG), where Vibrio cholerae is a non-toxigenic Vibrio cholerae mutant strain, and Salmonella is an attenuated Salmonella typhimurium strain.
Preferred Composition: C1 further comprises a delivery agent from bupivacaine, liposome and cationic lipid, and an adjuvant.

L34 ANSWER 5 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-362245 [39] WPIDS
DNC C2002-102513
TI South African Arbovirus genomic RNA, useful for producing defective infectious alpha viral particle, comprises nonstructural protein coding sequences encoding attenuating mutation and heterologous **nucleotide** sequence.
DC B04 D16
IN HEISE, M T; JOHNSTON, R E; SIMPSON, D
PA (UYNC-N) UNIV NORTH CAROLINA
CYC 97
PI WO 2002020721 A2 20020314 (200239)* EN 90p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001090642 A 20020322 (200251)
ADT WO 2002020721 A2 WO 2001-US27644 20010906; AU 2001090642 A AU 2001-90642 20010906
FDT AU 2001090642 A Based on WO 200220721
PRAI US 2000-230663P 20000907
AB WO 200220721 A UPAB: 20020621
NOVELTY - A South African Arbovirus No. 86 (S.A.AR86) genomic RNA (I), comprising a S.A.AR86 nonstructural protein (nsp) coding sequences encoding an attenuating mutation and a heterologous **nucleotide** sequence, is new.
DETAILED DESCRIPTION - A South African Arbovirus No. 86 (S.A.AR86) genomic RNA (I), comprising:
(a) a heterologous **nucleotide** sequence; and
(b) S.A.AR86 nonstructural protein (nsp) coding sequences encoding attenuating mutation chosen from:
(i) an attenuating mutation in the cleavage domain between the nsp1 and nsp2 coding sequences;
(ii) an attenuating mutation that results in a termination codon at nsp3 amino acid position 537;
(iii) an attenuating mutation comprising a substitution mutation at nsp3 amino acid position 385;

(iv) an attenuating mutation comprising an insertion of at least 8 amino acids following nsp3 amino acid position 385; and

(v) their combinations, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) an infectious (defective) **alpha -virus** particle (II) comprising **alpha -virus** structural proteins, and (I) packaged within the assembled **alpha -virus** structural proteins;

(2) a composition (III) comprising (II);

(3) a pharmaceutical formulation comprising (II), where the heterologous **nucleotide** sequence encodes an immunogenic polypeptide;

(4) a helper cell (IV) for packaging **alpha -virus** particles, comprising in an **alpha -virus**-permissive cell, (I) and one or more helper sequences encoding an **alpha -virus** structural proteins that are not encoded by the replicon RNA;

(5) a **DNA** molecule (V) comprising a segment encoding (I) and a promoter operatively associated with the segment encoding (I);

(6) an infectious RNA transcript encoded by (V);

(7) a vector (VI) comprising (V);

(8) a cell comprising (VI); and

(9) composition comprising several infectious, defective **alpha -virus** particles produced by using (IV).

ACTIVITY - Cytostatic; Virucide; Hemostatic; Anti-HIV; Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Antianemic; Antidiabetic; Ophthalmological.

MECHANISM OF ACTION - Elicitor of immune response. Four to six week old CD-1 were inoculated subcutaneously in the left rear footpad with 10 to the power of 4 infectious units (iu) of S.A.AR86 replicon expressing the hemagglutinin (HA) of influenza virus. Replicons contained either Ile (REP91HA) or Thr (REP89HA) at nsp1 538. Serum was harvested from the immunized mice at 12 weeks post inoculation and evaluated for anti-HA antibody using a HA specific enzyme linked immunosorbant assay (ELISA). Both replicons elicited an anti-HA response, however, the level of anti-HA response was consistently higher in animals immunized with REP91HA. Additional studies were performed to directly assess the ability of REP91HA vs REP89HA to induce antibody responses. Adult CD-1 mice were inoculated with 10 to the power of 4 iu of REP91HA or REP89HA. 12 weeks after the initial inoculation, mice were boosted with 10 to the power of 4 iu of REP91HA or REP89HA. Mice were sacrificed 10 days post boost and the number of antigen specific antibody secreting cells in the spleen was evaluated using a HA specific Elispot assay. REP89HA (nsp1 538 Thr) immunization induced an average of 2.8 plus or minus 2.2 HA specific antibody cells/10 to the power of 5 spleen cells. In contrast, REP91HA (nsp1 538Ile) induced 34.8 plus or minus 17 HA specific antibody secreting cells/10 to the power of 5 spleen cells. So immunization with a replicon encoding the Ile at nsp1 position 538 resulted in an increase of approximately 12 fold in the number of antigen specific antibody secreting cells compared to mice immunized with the wild type S.A.AR86 replicon encoding Thr at nsp1 position 538. This data demonstrated that in addition to increasing the safety of S.A.AR86 based vectors by attenuating S.A.AR86 for adult mouse neurovirulence, the presence of Ile at nsp1 position 538 also enhanced the humoral immune response generated against the heterologous gene encoded by the S.A.AR86 vector.

USE - (II) is useful for introducing a **nucleotide** sequence into a subject or a cell such as connective tissue cell, tendon cell, bone cell, a cell in the periosteum, bone marrow cell, cell in the endosteum, osteoclast, a cell within the epiphyses of a long bone, where the long bone is adjacent to an articular joint or their combinations. The cell is

then administered to a subject e.g. human, non-human primate, equine, bovine, ovine, caprine, porcine, feline, canine, murine or lagamorph subject. (III) is useful for producing an immune response in a subject. (IV) is useful for making an infectious, defective **alpha -virus** particle, by producing **alpha -virus** particles in the helper cell and collecting the particles produced by the helper cell, where the combined expression of the S.A.AR86 replicon RNA and the helper sequence(s) produces an assembled **alpha -virus** particle comprising the S.A.AR86 replicon RNA packaged within the **alpha -virus** structural proteins, and further the assembled **alpha -virus** particle is able to infect an **alpha -virus** permissive cell but is unable to propagate by producing new **alpha -virus** particles in the cell in the absence of helper sequences (all claimed). (III) provides an immune response against chronic or latent infective agents, including hepatitis B, C, Epstein-Barr Virus, herpes viruses, human immunodeficiency virus, and human papilloma virus, cancers including leukemia, lymphomas, colon cancer, renal and breast cancer. The heterologous polypeptide in (I) is a therapeutic polypeptide including those used in treatment of disease condition including, cystic fibrosis, hemophilia A, B, thalassemia, anemia and the other blood disorders, acquired immunodeficiency syndrome (AIDS), Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, epilepsy, and other neurological disorders, cancers, diabetes mellitus, muscular dystrophies, Gaucher's disease, Hurler's disease, adenosine deaminase deficiency, glycogen storage diseases and other metabolic defects, retinal degenerative diseases (and other diseases of other metabolic defects), retinal degenerative diseases, and diseases of solid organs.

ADVANTAGE - The attenuating mutation does not result in a significant reduction in transgene expression from the attenuating **alpha -virus** genomic RNA, i.e. transgene expression is essentially the same as in non-attenuated viruses. Transgene expression is enhanced in the attenuated virus as compared with the non-attenuated virus.

Dwg.0/8

TECH UPTX: 20020621

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Nucleic Acid**: (I) further comprises a promoter that is operatively associated with the heterologous **nucleotide** sequence. (I) comprises an attenuating mutation in the cleavage domain between the nsp1 and nsp2 coding sequences comprising a substitution mutation at nsp1 amino acid position 538, or a mutation that results in an opal termination codon at nsp3 amino acid position 537, a substitution mutation at nsp3 amino acid position 385, and insertion of the amino acid sequence (S) of Ile-Thr-Ser-Met-Asp-Ser-Trp-Ser-Ser-Gly-Pro-Ser-Ser-Leu-Glu-Ile-Val-Asp or at least 8 contiguous amino acids of (S) following nsp3 amino acid position 385. (I) further comprises an **alpha-virus** capsid enhancer sequence operatively associated with the heterologous **nucleotide** sequence, and expresses a **fusion** protein comprising a polypeptide encoded by the heterologous **nucleotide** sequence and a polypeptide encoded by the capsid enhancer sequence. (I) also comprises a segment encoding an exogenous **protease** which is a foot and mouth disease virus 2A **protease**. The **alpha-virus** capsid enhancer sequence, the segment encoding the exogenous **protease** and heterologous **nucleotide** sequence are in the 5'-3' direction. The capsid enhancer sequence is a S.A.AR86 capsid enhancer sequence, and comprises a coding sequence for an amino terminal portion of an **alpha-virus** capsid protein. The **alpha-virus** capsid enhancer sequence is operably associated with the heterologous **nucleotide** sequence, so that

expression of the heterologous **nucleotide** sequence is enhanced as compared to the level of expression in the absence of the capsid enhancer sequence. (I) is a replicon molecule that does not express one of the S.A.AR86 structural proteins, S.A.AR86E1 or S.A.AR86E2 glycoprotein or both, or S.A.AR86 capsid protein. The sequences encoding the non-expressed S.A.AR86 structural protein(s) have been deleted from the replicon molecule. The heterologous **nucleotide** sequence encodes an immunogenic or therapeutic polypeptide.
Preferred Cell: In (IV), one or more helper sequences are stably incorporated into the genome of the helper cell and only encode the **alpha-virus** structural proteins that are not provided by the replicon RNA. The replicon RNA is expressed from a **DNA** sequence that has been introduced into the helper cell. The **DNA** sequence is a plasmid or viral vector and is stably incorporated into the genome of the helper cell. The replicon RNA is introduced into the helper cell by electroporation, the helper sequences are RNA sequences that are introduced into the helper cell by electroporation or both. The helper sequences lack a **alpha-virus** packaging sequence.

L34 ANSWER 6 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-269094 [31] WPIDS
DNC C2002-079859
TI New autofluorescent **fusion** protein, useful for determining **protease** and **protease**-inhibiting activity, comprises two different proteins linked by **protease** cleavage site.
DC B04 D16
IN KETTLING, U; KOLTERMANN, A; KUHLEMANN, R; SCHWILLE, P
PA (DIRE-N) DIREVO BIOTECH AG
CYC 96
PI WO 2002012543 A2 20020214 (200231)* DE 35p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 10038382 A1 20020221 (200231)
AU 2001083988 A 20020218 (200244)
ADT WO 2002012543 A2 WO 2001-EP9112 20010807; DE 10038382 A1 DE 2000-10038382 20000807; AU 2001083988 A AU 2001-83988 20010807
FDT AU 2001083988 A Based on WO 200212543
PRAI DE 2000-10038382 20000807
AB WO 200212543 A UPAB: 20020516
NOVELTY - Autofluorescing **fusion** protein (I) comprises:
(i) first autofluorescing protein (Ia);
(ii) segment containing a **protease** cleavage site; and
(iii) at least one different autofluorescing protein (Ib).
Essentially no fluorescent energy transfer occurs between (Ia) and (Ib).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) nucleic acid sequence (II) that encodes (I);
(2) vector containing (II);
(3) cells or transgenic organisms containing (II) and/or the vector of (2);
(4) recombinant production of (I) by expressing (II) in cellular or cell-free systems;
(5) analyzing a sample for **protease**, or **protease**-inhibiting activity; and
(6) analyzing intracellular **protease**, or **protease**

-inhibiting activity.
USE - (I) is used for detecting and quantifying **protease** (or **protease**-inhibitory) activity in liquid samples or cells, particularly for screening-based optimization (or generation) of biomolecules with proteolytic activity.
ADVANTAGE - (I) can be prepared in cellular or cell-free systems and makes possible intracellular analysis of **protease** activity. Preparation of (I) does not require regioselective coupling of fluorophores to polypeptides and any selected **protease** cleavage site can be incorporated.
Dwg.0/5

TECH UPTX: 20020516
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Fusion** Proteins: Segment (ii) is:
(a) positioned between (Ia) and (Ib), which have different spectral properties; and/or
(b) includes a terminal linker peptide as well as the cleavage site, and/or
(c) is at least 10, preferably, 30 amino acids long.
The cleavage site is specific for:
(i) the **protease** of human immune deficiency **virus**, hepatitis C **virus**, tobacco etch **virus** (TEV), human cytomegalovirus or herpes simplex **virus**; or
(ii) plasmin, angiotensin converting enzyme, tissue plasminogen factor and/or thrombin. (Ia) is green fluorescent protein (GFP) from Aequorea victoria, particularly a red-shifted variant (rsGFP), and (Ib) is dsRed from Discosoma sp., or its variants.
(I) may include other functional **peptide** sequences, e.g. **signal**, affinity or detectable marker peptides. The specification includes two sequences for (I) of 506 and 547 amino acids; both contain rsGFP and dsRed, linked via 32 or 73 amino acid peptides that include the recognition site for TEV **protease**.
Preferred process: In method (6), (I) and test sample are combined in aqueous solution, incubated, then the amount of cleaved (I) determined by (two-color) confocal fluorimetry, particularly fluorescence cross-correlation spectrometry; confocal fluorescence coincidence analysis or two-dimensional fluorescence intensity distribution analysis. Method (6) is essentially the same but includes introduction of (II) and/or a vector into cells so that (I) is expressed within the cell.
Preparation: (I) isolated by standard genetic recombinant methods.

L34 ANSWER 7 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-257913 [30] WPIDS
DNC C2002-076795
TI Selecting exogenous **nucleic acids** having a desired feature, particularly from a library of **nucleic acids**, involves using a **viral genome**.
DC B04 D16
IN LANCTOT, C; MOFFAT, P; SALOIS, P
PA (PHEN-N) PHENOGENE THERAPEUTIQUES INC
CYC 97
PI WO 2002016572 A2 20020228 (200230)* EN 87p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001087396 A 20020304 (200247)
ADT WO 2002016572 A2 WO 2001-CA1169 20010817; AU 2001087396 A AU 2001-87396

20010817
FDT AU 2001087396 A Based on WO 200216572
PRAI US 2000-641931 20000818
AB WO 200216572 A UPAB: 20020513
NOVELTY - Use of a **viral genome** for selecting an exogenous **nucleic acid** having a desired feature, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) selecting a **nucleic acid** having a desired feature, comprising:

(a) providing a **viral genome** capable of expressing an exogenous **nucleic acid** inserted into it, when in a suitable host, and also capable of packaging itself into a viral particle;

(b) providing a **suppressive condition** where the **viral genome** is capable of packaging itself into a viral particle only once the **suppressive condition** is being overcome;

(c) inserting an exogenous **nucleic acid** into the **viral genome** to provide a recombinant **viral genome**;

(d) **transfecting** the genome into a host; and

(e) allowing the genome to express the exogenous **nucleic acid** and package itself into a recombinant viral particle, the production of at least one recombinant viral particle indicates that the **suppressive condition** has been overcome, and the exogenous **nucleic acid** has he desired feature;

(2) selecting from a library of **nucleic acid**, a **nucleic acid** having a desired feature, comprising:

(a) providing a **viral genome** capable of expressing an exogenous **nucleic acid** inserted into it, capable of autoreplication and also capable of packaging copies of itself into viral particle;

(b) providing a **suppressive condition** where the **viral genome** is capable of autoreplication or producing a viral particle capable of infecting a host only once the **suppressive condition** has been overcome;

(c) inserting an exogenous **nucleic acid** from the library into the **viral genome** to provide a recombinant **viral genome**;

(d) **transfecting** the genome into a host; and

(e) allowing the recombinant **viral genome** to express the exogenous **nucleic acid**, autoreplicates and package copies of itself into recombinant viral particles;

(3) selecting from a library of **nucleic acids**, a **nucleic acid** having a desired feature, comprising:

(a) providing a plasmid comprising a **viral genome**, when present in a host:

(i) expressing an exogenous **nucleic acid** inserted into it;

(ii) packaging the exogenous **nucleic acid** into a recombinant viral particle

(b) inactivating the packaging ability of the **viral genome**, and inserting from the library an exogenous **nucleic acid** into the **viral genome** to provide a recombinant **viral genome**;

(c) producing copies of the recombinant **viral genome**;

(d) **transfecting** the copies into a host; and

(e) allowing the genome to express the exogenous **nucleic acid** and package itself into a recombinant viral particle;

(4) selecting a **nucleic acid** encoding a **protease**, comprising:

(a) providing a **viral genome** modified to encode a **fusion** protein comprising a structural viral protein bound to a **fetter** protein, where production of a particle is dependent on the liberation of the structural viral protein from the **fetter** -protein;

(b) inserting an exogenous **nucleic acid** into the **viral genome**;

(c) **transfecting** the genome into a host; and

(d) allowing the genome to express the exogenous **nucleic acid** and package itself into a recombinant viral particle;

(5) selecting a **nucleic acid** encoding a protein with drug-resistant activity, or a protein cleavage site comprising:

(a) providing a **viral genome** encoding a **viral** particle, which:

(i) expresses an exogenous nucleic acid inserted into it; and

(ii) packages the nucleic acid into a viral particle;

(b) inserting an exogenous nucleic acid into the genome;

(c) transfecting the genome into a suitable host;

(d) exposing the host transfected in (c) to a substance inhibiting viral packaging function; and

(e) allowing the genome to express the exogenous nucleic acid and package itself into a recombinant viral particle;

(6) an isolated nucleic acid encoding a dysfunctional viral genome, where production of a viral particle is dependent on insertion of an exogenous nucleic acid, and introduction of the nucleic acid having incorporated the exogenous nucleic acid;

(7) an isolated nucleic acid molecule encoding a dysfunctional viral genome, where production of an infectious viral particle from the nucleic acid is dependent on insertion of an exogenous sequence encoding a protein with a protease substrate cleavage site, and introduction of the nucleic acid into a host;

(8) a kit for selecting a nucleic acid with a desired feature, comprising an isolated nucleic acid molecule encoding a dysfunctional viral genome, and at least one further element selected from instructions for use, reaction buffers, enzymes, probes, or pools of exogenous nucleotide sequences; and

(9) an isolated or purified N-terminal amino acid sequence encoding a dysfunctional signal peptide of a viral envelope protein, having the characteristics of allowing the viral envelope proteins association without directing the viral envelope protein into the cellular secretory pathway and across the lipid bilayer of a host cell.

USE - For selecting an exogenous nucleic acid, particularly from a library of nucleic acids, having a desired feature (claimed).

ADVANTAGE - The method removes the expensive and time-consuming task of selecting cells that express a gene of interest. The method is more rapid, efficient and accurate for selecting a particular nucleic acid having a desired feature, characteristic or function.

Dwg.0/0

TECH UPTX: 20020513

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In the method of (1), the desired feature is a **nucleic acid** encoding a **protease**, a **signal peptide**, or a drug-resistant protein. The **suppressive condition**, comprises:

(a) modifying the **viral genome** to inactivate a **viral** gene product involved in the packaging of the viral

particle; or
(b) exposing the host to a substance inhibiting viral packaging function.
The exogenous **nucleic acid** is devoid of a termination
codon in frame and downstream of a translation start site. The
viral genome is modified to encode a dysfunctional
signal peptide of a viral envelope protein, or encodes a
fusion protein having a structural viral protein bound to a
fetter-protein. The **fetter**-protein blocks the packaging
function of the structural protein essential for viral packaging function.
The method further comprises the step of exposing the host to a substance
inhibiting viral packaging function. The **viral genome**
transfected into the suitable host in RNA form. The **viral**
genome is in cDNA form and is incorporated into a vector,
preferably a plasmid or bacteriophage. The exogenous **nucleic**
acid is taken from a library of **nucleic acids**.
The **viral genome** encodes an **alphavirus**,
preferably a **sindbis** or Semliki Forest **virus**. The
viral genome is capable of autoreplication an insertion
of an exogenous sequence results in the production of a clonal population
of recombinant viral particles. The particles are preferably infectious.
The method further comprises:
(a) isolating the recombinant viral particle;
(b) propagating the particle;
(c) identifying a biological function for the **nucleic**
acid;
(d) identifying a protein encoded by the exogenous **nucleic**
acid; and
(e) sequencing at least partially the exogenous **nucleic**
acid found in the particle.
In the method of (2), the **viral genome** is modified to
abolish autoreplication function and/or infectivity of viral particles
produced from them. The expression of an exogenous **nucleic**
acid having a desired feature restores the functions and/or
infectivity. In the method of (4), the exogenous **nucleic**
acid is devoid of a termination codon in frame and downstream of a
translation start site. The **viral genome** has been
modified to render dysfunctional a **signal peptide** of a
viral envelope protein. The **signal peptide** dysfunction
does not affect viral envelope protein association. The **viral**
genome is incorporated into a vector in a cDNA form.
Preferred **Nucleic Acid**: The **nucleic**
acid has a 51, 148, 18, 54 or 48 **nucleotide** sequence,
all given in the specification.

L34 ANSWER 8 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-188753 [24] WPIDS
DNC C2002-058414
TI New **nucleic acid** construct for detecting anti-viral
drugs, comprises a **polynucleotide** cassette encoding a
chimeric polypeptide with two polypeptide sequences and a
protease recognition site cleavable by a virally encoded
protease.
DC B04 D16
IN APPEL, E
PA (AMID-N) AMIDUT LTD
CYC 96
PI WO 2002010430 A2 20020207 (200224)* EN 93p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001082437 A 20020213 (200238)

ADT WO 2002010430 A2 WO 2001-IL702 20010730; AU 2001082437 A AU 2001-82437 20010730

FDT AU 2001082437 A Based on WO 200210430

PRAI US 2000-629969 20000731

AB WO 200210430 A UPAB: 20020416

NOVELTY - A **nucleic acid** construct (I) comprising a **polynucleotide** cassette (II) encoding a **chimeric** polypeptide comprising a first polypeptide sequence, a second polypeptide sequence translationally fused to the first sequence, and a **protease** recognition site (PRS) cleavable by a virally encoded **protease**, where cleavage of the PRS leads to a detectable signal, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a recombinant virus genome (III) comprising (I);

(2) a transformed cell including (I);

(3) a **nucleic acid** construct (Ia) comprising at least a portion of a first genome of a first virus comprising a **polynucleotide** sequence encoding a **chimeric** polypeptide having a PRS cleavable by a **protease** encoded by a second genome of a second virus, where a portion of the first genome of the first virus is capable of replicating only in a cell expressing the **protease** encoded by the second genome of the second virus;

(4) a **nucleic acid** construct (Ib) comprising a **polynucleotide** cassette encoding a **chimeric** polypeptide including a reporter polypeptide sequence, and a PRS polypeptide sequence being integrated within the reporter polypeptide sequence, where the PRS is cleavable by a virally encoded **protease**, and cleavage of the PRS leads to abolishment of a reporter function of the reporter polypeptide;

(5) a **chimeric** polypeptide (IV) comprising a first polypeptide sequence, a second polypeptide sequence linked to the first sequence, and a PRS cleavable by a virally encoded **protease**, where cleavage of the PRS leads to a detectable signal; and

(6) detecting (M) the presence of a virus in a cell, by introducing into the cell, or incubating with an extract of the cell, (II), and measuring the detectable signal or reporter function.

ACTIVITY - Antiviral. No biological data is given.

MECHANISM OF ACTION - None given.

USE - (I), or one of two other **nucleic acid** constructs (Ia or Ib) is useful for uncovering molecules having antiviral activity or for determining viral drug resistance, by providing a cell infected with a virus encoding a viral **protease**, introducing into the cell a molecule with potential anti-viral activity or an anti-viral drug and (I), (Ia) or (Ib), and measuring the detectable signal, measuring a degree of lysis of the cells, or measuring the reporter function. (Ia) is introduced into cells infected with a first virus encoding a viral **protease**, and (Ia) includes at least a portion of a genome of a second virus comprising a **polynucleotide** sequence encoding a PRS cleavable by the viral **protease**, and the second virus is capable of replicating and lyzing the cells upon cleavage of PRS. The method further comprises comparing the detectable signal to that from cells not infected with the virus and/or to the cells not including the molecule with potential anti-viral activity, or comparing the degree of lysis to that detected in cells infected with the first virus yet not including the molecule, where the degree of lysis is

measured as a function of time. The method further comprises comparing the detectable signal, degree of lysis or measured reporter function to that from cells infected with the virus yet devoid of the anti-viral drug. (Ib) is useful for detecting the presence of a first virus in cell, by introducing (Ib) in the cells, and measuring degree of lysis of the cells. A new **chimeric** polypeptide (IV) is useful for detecting the presence of a virus in a cell, for determining viral drug resistance, and for uncovering molecules having antiviral activity, by incubating (I) with an extract of the cell, and measuring the detectable signal (all claimed). (I) is useful for detecting viral encoded **protease** found in infected cells or their extracts to detect the presence or absence of viral infection. (I) is useful for phenotypic testing of human immunodeficiency virus (HIV) drug resistance.

ADVANTAGE - (I) enables screening of molecules in an easy and rapid manner. The methods which use (I) are easy to implement and execute, and when (I) is utilized for uncovering potential viral drugs and for drug resistance screening it provides accurate results which far exceeds that achieved by presently available in vitro methods. (I) efficiently detects the presence of viral **protease** and viral particles within cells. (I) is specific, sensitive and lacks background enzymatic activity in the absence of human immunodeficiency virus (HIV) **protease**, and is suitable for detection of specific viral strain isolates even under low viral load conditions. When used for phenotypic testing of HIV drug resistance, (I) eliminates the need to determine the titer of the virus, and delivers accurate results within 24 hours.

Dwg.0/24

TECH UPTX: 20020416

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Construct: In (I), at least one PRS is interposed between the first and the second polypeptide sequences. The **chimeric** polypeptide further includes a third polypeptide sequence being translationally fused to the second polypeptide sequence. (I) further comprises a promoter sequence for directing the transcription of (II), where the promoter sequence is functional in a eukaryotic cell e.g., a mammalian cell. (I) further comprises at least one **polynucleotide** sequence derived from a coding or non-coding region of a virus genome. The first and second polypeptide sequence encodes a protein selected from enzyme, substrate protein, ligand protein and a fluorophore protein. The first polypeptide sequence encodes a first fluorophore protein such as green fluorescence protein, and the second polypeptide sequence encodes a second fluorophore protein such as blue fluorescence protein.

Preferred Virus: (III) is an **alpha virus**.

Preparation: (I) is prepared by standard recombinant techniques.

L34 ANSWER 9 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-130880 [17] WPIDS
DNC C2002-040258
TI New polynucleotide encoding antimicrobial peptide termicin, useful e.g. as fungicide, for clinical use or for plant protection, particularly expressed by transgenic plants.
DC B04 C06 D16 P13
IN BULET, P; HOFFMANN, J; LAMBERTY, M; LATORSE, M P; LATORSE, M
PA (RHOB-N) RHOBIO SA; (RHOB-N) RHOBIO
CYC 96
PI WO 2002000706 A2 20020103 (200217)* FR 34p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU

SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2810993 A1 20020104 (200217)
AU 2001070669 A 20020108 (200235)
ADT WO 2002000706 A2 WO 2001-FR2028 20010627; FR 2810993 A1 FR 2000-8374 20000629; AU 2001070669 A AU 2001-70669 20010627
FDT AU 2001070669 A Based on WO 200200706
PRAI FR 2000-8374 20000629
AB WO 200200706 A UPAB: 20020313
NOVELTY - An isolated polynucleotide (I) that encodes a termicin, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(a) antimicrobial peptides (II), of the defensin family, encoded by (I);
(b) **chimeric** gene (CG) containing, operably linked, promoter, (I) and terminator;
(c) expression or transformation vector containing CG;
(d) host organism transfected with the vector of (c);
(e) transformed plant cells and plants (or their parts and seeds) that contain CG; and
(f) production of (II) by growing cells of (d) and (e).
ACTIVITY - Antibiotic; fungicide. Termicin had typical MIC (undefined) values (micro M) of 0.2-0.4 against Neurospora crassa and Fusarium culmorum and 6-12 against Candida albicans and Cryptococcus neoformans.
MECHANISM OF ACTION - None given in the source material.
USE - (I) is used to produce recombinant termicin, useful as a fungicide (also active against Gram-positive bacteria) in human and veterinary medicine and for production of transgenic plants that are resistant to a wide range of fungi.
Dwg.0/0
TECH UPTX: 20020313
TECHNOLOGY FOCUS - BIOLOGY - Preparation: Imagines of the termite Pseudacanthotermes spiniger were inoculated with Micrococcus luteus and Escherichia coli, grown for 24 hour, then extracted with trifluoroacetic acid, containing inhibitors of **protease** and melanin formation. The extract was pre-purified on a C18 column then purified by reverse-phase high-performance liquid chromatography on Aquapore RP-300 C8; size-exclusion chromatography on Ultraspherogel SEC300; chromatography on Aquapore OD-300 and chromatography on DeltaPak HPIC18. The structure of the purified peptide was determined by mass spectrometry, Edman sequencing etc. It was: ACNFQSCWATCQAQHSIYFRRAFCDRSQCKCVFVRG (S2).

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Nucleic Acid: (I): (i) encodes peptide (S2); (ii) hybridizes to (i); (iii) is homologous to (i) or (ii); or (iii) is a fragment of (i)-(iii). Especially (I) is a fully defined sequence of 112 base pairs (bp) as given in the specification.
Preferred Construct: In CG, the promoter is constitutive or inducible and CG may also include a **signal** or transit **peptide** encoding sequence. It is particularly used to transform a microorganism (Escherichia coli; yeasts of the genera Saccharomyces, Kluyveromyces and Pichia, or baculovirus); a plant cell or a plant. Suitable vectors for CG are plasmids, phages and **viruses**. Once the sequence for (II) has been identified, it can be synthesized conventionally and expressed form usual vector/host systems.

TECHNOLOGY FOCUS - AGRICULTURE - Preferred Plant: These are resistant to Cercospora, especially C. fijensis; Septoria, especially S. nodorum or S. tritici; Fusarium, especially F. nivale or F. graminearum; Botrytis,

especially B. cinerea and Rhizoctonia, especially R. solani.
Preferred Process: Transgenic plants that express (II) are grown conventionally and may be treated with a composition containing at least one fungicide and/or bactericide, especially one that complements the activity of (II).

L34 ANSWER 10 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-602251 [68] WPIDS
DNC C2001-178322
TI Non-naturally occurring gene therapy vector useful for gene therapy, comprises an inner shell having a core complex containing a **nucleic acid** and at least one complex forming reagent.
DC A96 B04 B05 D16
IN CHENG, C; FREI, J; METT, H; PUTHUPPARAMPIL, S; STANEK, J; SUBRAMANIAN, K; TITMAS, R; WOODLE, M; YANG, J
PA (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH
CYC 95
PI WO 2001049324 A2 20010712 (200168)* EN 178p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001033669 A 20010716 (200169)
EP 1242609 A2 20020925 (200271) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001049324 A2 WO 2000-EP13300 20001228; AU 2001033669 A AU 2001-33669 20001228; EP 1242609 A2 EP 2000-991644 20001228, WO 2000-EP13300 20001228
FDT AU 2001033669 A Based on WO 200149324; EP 1242609 A2 Based on WO 200149324
PRAI US 1999-475305 19991230
AB WO 200149324 A UPAB: 20011121
NOVELTY - A non-naturally occurring gene therapy vector, comprising an inner shell having a core complex (1) containing a **nucleic acid** and at least one complex forming reagent (2), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) forming a self assembling core complex by feeding a stream of a solution of a **nucleic acid** and a core complex-forming moiety into a static mixer, the streams are split into inner and outer helical streams that intersect at several different points causing turbulence and promoting mixing, that results in a physicochemical assembly interaction; and
(2) a compound having formula (I).
m = 3 or 4;
Y = -(CH2)n-, or -CH2-CH=CH-CH2- if R2 is -(CH2)3-NR4R5 and m is 3;
n = 3-16;
R2 = H, or lower alkyl, or -(CH2)3-NR4R5 is m is 3;
R3 = H, or alkyl, or -CH2-CH(-X')-OH if R2 is -(CH2)3-NR4R5 and m is 3;
X and X' = independently, H or alkyl; and
R, R1, R4 and R5 = independently, H or lower alkyl, where R, R1, R4 and R5 are not all H or methyl, if m is 3 and Y is -(CH2)3.
ACTIVITY - None given.
MECHANISM OF ACTION - Gene therapy.
No biological data is given.
USE - In gene therapy for **nucleic acid** delivery.
ADVANTAGE - The vectors are stable having an improved outer steric layer that provides enhanced target specificity, in vivo and colloidal

stability. The vectors are relatively homogenous and comprises chemically defined species. The vectors demonstrate improved cell entry and intracellular trafficking, permitting enhanced **nucleic acid** therapeutic activity such as gene expression.
Dwg.0/30

TECH UPTX: 20011121

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The vector further comprises a fusogenic moiety, an outer shell moiety and a targeting moiety. The vector comprises a mixture of at least two outershell reagents in which each of the outershell reagents comprises the hydrophilic polymer having substantially different sizes. The fusogenic moiety is incorporated directly in (1) and comprises a shell that is anchored to (1). The fusogenic moiety comprises at least one moiety selected from a viral peptide, an amphiphilic peptide, a fusogenic polymer lipid conjugate and a biodegradable fusogenic polymer-lipid conjugate. The fusogenic moiety is a membrane surfactant polymer-lipid conjugate selected from Thesit (RTM), Brij 58 (RTM), Brij 78 (RTM), Tween 80 (RTM), Tween 20 (RTM), C12E8, C14E8, C16E8, Chol-PEG 900, analog containing polyoxazoline or other hydrophilic polymer substituted for the PEG and analog having fluorocarbons substituted for the hydrocarbon.
CnEn = hydrocarbon poly(ethylene glycol) ether;
C = hydrocarbon of carbon length N; and
E = poly(ethylene glycol) of degree of polymerization N.
The inner shell is anchored to the outer shell moiety via a covalent linkage that is degradable by chemical reduction or sulfhydryl treatment at a pH of at most 6.5. The covalent linkage is selected from -C(O)-NH-N=CH-, -C(O)-NH-NH-C(O)-NH=CH-, -O-T-CH=N-NH-C(O)- or -NH-C(O)-CH2-CH2-S-S-. The outer shell moiety stabilizes the vector and reduces nonspecific binding to proteins and cells. The outer shell moiety is anchored to the fusogenic moiety and (1) and comprises a hydrophilic polymer. The outer shell comprises the targeting moiety. The outer shell comprises a protective polymer conjugate in which the polymer exhibits solubility in both polar and non-polar solvents. The targeting moiety enhances binding of the vector to a target tissue and cell population. The targeting element is a receptor ligand, an antibody or antibody fragment, a targeting peptide, a targeting carbohydrate molecule or a lectin, preferably vascular endothelial cell growth factor, fibroblast growth factor (FGF)2, somatostatin and its analog, transferrin, melanotropin, ApoE and ApoE peptide, von Willebrand's Factor and von Willebrand's Factor peptide; adenoviral fiber protein and adenoviral fiber protein peptide; PD1 and PD1 peptide, epidermal growth factor (EGF) and EGF peptide, RGD peptide, folate, pyridoxyl, sialyl-Lewis and chemical analogs. (2) is selected from a lipid, a polymer, and a spermine analog complex of (I). The complex-forming lipid agent is selected from phosphatidylcholine, phosphatidylethanolamine, dioleoylphosphatidylethanolamine, dioleoylphosphatidylcholine, cholesterol and other sterols, N-1-(2,3-dioleyloxy)propyl-N,N,N-trimethylammonium chloride, 1,2-bis(oleoyloxy)-3-(trimethylammonia) propane, phosphatidic acid, phosphatidylglycerol, phosphatidylinositol, glycolipids comprising two optionally unsaturated 14-22C hydrocarbon chains, sphingomyelin, sphingosine, ceramide, terpenes, cholesterol hemisuccinate, cholesterol sulfate, diacylglycerol, 1,2-dioleoyl-3-dimethylammonium propanediol, dioctadecyldimethylammonium bromide, dioctadecyldimethylammonium chloride, dioctadecylamidoglycylspermine, 1,3-dioleoyloxy-2-(6-carboxyspermyl)propylamide, Lipofectamine7 (RTM) (2,3-dioleyloxy-N-(2-(sperminecarboxamido)ethyl)-N,N-dimethyl-1-propanaminium trifluoroacetate), hexadecyltrimethyl-ammonium bromide, dimethyl-dioctadecylammonium bromide, 1,2-dimyristyloxypropyl-3-dimethyl-hydroxy ethyl ammonium bromide, dipalmitoylphosphatidylethanolamylspermine , dioctylamineglycinespermine, dihexadecylamine-spermine (C18-2-Sper),

aminocholesterol-spermine, 1-(2-(9(Z)-octadecenoyloxy)ethyl)-2(8(Z)-heptadecenyl)-3-(2-hydroxyethyl)imidazolinium chloride, dimyristoyl-3-trimethylammonium-propane, 1,2-dimyristoyl-sn-glycero-3-ethylphosphatidylcholine, lysylphosphatidylethanolamine, cholestryl-4-aminoproprionate, Genzyme-67 (spermadine cholestryl carbamate), 2-(dipalmitoyl-1,2-propandiol)-4-methylimidazole, 2-(dioleoyl-1,2-propandiol)-4-methylimidazole, 2-(cholestryl-1-propylamine carbamate)imidazole, N-(4-pyridyl)-dipalmitoyl-1,2-propandiol-3-amine, 3-beta-(N-(N',N'- dimethylaminoethane)carbamoyl)cholesterol, 3beta-(N-(N',N',N'-trimethylaminoethane)carbamoyl) cholesterol, 1,2-dioleoyl-sn-glycero-3-succinate, 1,2-dioleoyl-sn-glycero-3-succinyl-2-hydroxethyl disulfide ornithine conjugate, 1,2-dioleoyl-sn-glycero-3-succinyl-2-hydroxethyl hexyl orithine conjugate, N,N',N,N'-tetramethyl-N,N',N,N'-tetrapalmityolspermine, 3-tetradecylamino-N-tert-butyl-N'-tetradecylpropionamidine (vectamidine or diC14-amidine), YKS-220 (RTM) (N-(3-(2-(1,3-dioleoyloxy)propoxy-carbonyl)propyl)-N,N,N-trimethyl ammonium iodide) and DC-6-14 (RTM) (O,O'-ditetradecanoyl-N-(alpha-trimethylammonioacetyl)diethanolamine chloride). (2) comprises a mixture of at least two (2). (2) possesses at least one additional activity selected from cell binding, biological membrane fusion, endosome disruption and nuclear targeting. The **nucleic acid** is selected from a recombinant plasmid, a replication-deficient plasmid, a mini-plasmid, a recombinant **viral genome**, a linear **nucleic acid** fragment, an antisense agent, a linear **polynucleotide**, a circular **polynucleotide**, a ribozyme, a cellular promoter and a **viral genome**. (2) further comprises a nuclear targeting moiety that enhances nuclear binding and/or uptake. The nuclear targeting moiety is selected from a nuclear localization **signal peptide**, a nuclear membrane transport peptide or a steroid receptor binding moiety. The nuclear targeting moiety is anchored to the **nucleic acid** in (1). The viral peptide is selected from MLV env peptide, HA env peptide, a viral envelope protein ectodomain, a membrane-destabilizing peptide of a viral envelope protein membrane-proximal domain, a hydrophobic domain peptide segment of a viral fusion protein or an amphiphilic-region containing peptide. The amphiphilic-region containing peptide is selected from melittin, magainins, fusion segments from Haemophillus influenza hemagglutinin (HA) protein, human immunodeficiency virus (HIV) segment I from the cytoplasmic tail of HIV 1gp41 or amphiphilic segments from viral env membrane proteins.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The fusogenic moiety comprises a fusogenic polymer, a fusogenic polymer lipid conjugate, a biodegradable fusogenic polymer or a biodegradable fusogenic polymer-lipid conjugate. (2) is a polymer of structure -(-N(R1)-CH2-R2-)x-(-N(R3)-CH2-R2-)y-. The fusogenic moiety is a polymer of structure -(-N(R1)-CH2-R2-)x-(-N(R'3)-CH2-R2-)y-.

R1 and R3 = hydrocarbon optionally substituted with amine, guanidinium or imidazole moiety;

R2 = lower alkyl;

x and y = not defined;

R'3 = hydrocarbon optionally substituted with carboxyl, hydroxyl, sulfate or phosphate.

The outer shell comprises a protective steric polymer conjugate in which the polymer is selected from the group consisting of polyethylene-glycol (PEG), a polyacetal polymer, a polyoxazoline polymer optionally block with end-group conjugation, a hydrolyzed dextran polyacetal polymer, a polyoxazoline, a polyethylene glycol, a polyvinylpyrrolidone, polylactic acid, polyglycolic acid, polymethacrylamide, polyethyloxazoline, polymethyloxazoline, polydimethylacrylamide, polyvinylinethylether, polyhydroxypropyl methacrylate, polyhydroxypropylmethacrylamide,

polyhydroxyethyl acrylate, polyhydroxyethyloxazoline, polyhydroxypropyloxazoline, polyaspartamide or a polyvinyl alcohol.

L34 ANSWER 11 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-522588 [57] WPIDS
DNC C2001-156046
TI Protein conjugate for treating viral infections, comprises a region containing a factor that permits protein translocation across cell membrane and a second region comprising a single chain antibody.
DC B04 D16
IN BROOKS, T J G; DUGGAN, J M
PA (MINA) UK SEC FOR DEFENCE
CYC 95
PI WO 2001060866 A1 20010823 (200157)* EN 33p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001032095 A 20010827 (200176)
EP 1261645 A1 20021204 (200280) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001060866 A1 WO 2001-GB586 20010214; AU 2001032095 A AU 2001-32095 20010214; EP 1261645 A1 EP 2001-904178 20010214, WO 2001-GB586 20010214
FDT AU 2001032095 A Based on WO 200160866; EP 1261645 A1 Based on WO 200160866
PRAI GB 2000-3284 20000215
AB WO 200160866 A UPAB: 20011005
NOVELTY - A new protein conjugate comprising:
(a) a first region containing a factor that permits translocation of a protein across a cell membrane; and
(b) a second region comprising a single chain antibody fragment having an affinity for a viral protein.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a **polynucleotide**, which encodes the protein conjugate;
(2) a vector comprising the **polynucleotide** of (1);
(3) a cell transformed with the vector capable of expressing a protein conjugate;
(4) a recombinant virus transformed with a vector capable of expressing the protein conjugate;
(5) a pharmaceutical composition comprising a protein conjugate, a **polynucleotide** of (1), a cell of (3), or a recombinant virus of (4), in combination with a carrier or diluent; and
(6) preparing a protein conjugate by culturing a cell of (3) and recovering the protein conjugate.
ACTIVITY - Antiviral. No biological data is given.
MECHANISM OF ACTION - Protein therapy.
USE - The protein conjugate is useful in antiviral therapy or in preparing a medicament for the treatment of viral infections, particularly those by flaviviruses and **alphaviruses**. The conjugate can penetrate an infected cell and deliver an antibody into the cell to target an essential protein of viral replication to inhibit replication.
Dwg.0/4
TECH UPTX: 20011005
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Conjugate: The first region comprises the homeodomain of antennapedia, or its functional fragment or homologue. The viral protein is a protein from a flavivirus, **alphavirus**, enterovirus, arbovirus, retrovirus, respiratory virus,

rhabdovirus, herpes virus, human papilloma virus, adenovirus, adenavirus or a pox virus. The protein conjugate is preferably a flavivirus selected from hepatitis c virus, dengue virus or tick-borne encephalitis virus. The viral protein is a non-structural protein and is a protein necessary for replication of the virus. The single-chain antibody fragment has affinity for a flavivirus non-structural protein, identified as NS1, NS2, NS3, NS4, NS4B, NS5a and NS5B. The viral protein may also be a structural protein, which is an E1, or E2 protein of an **alphavirus**. The protein conjugate further comprises a therapeutic agent and an intracellular localization group. The protein conjugate is in the form of a **fusion** protein. The first and second region and/or any therapeutic agent present and/or an intracellular localization group are spaced by a spacer amino acid sequence, which includes a cleavage site of an intracellular enzyme. The protein conjugate recovered is purified under non-denaturing conditions, and is refolded prior to use. Recovery is effected in the presence of a **protease** inhibitor.
Preferred Cell: The cell is comprised of a gut-colonizing organism, preferably an attenuated Salmonella.
Preferred Virus: The recombinant virus is an attenuated vaccinia virus.
Preferred Composition: The composition comprises a therapeutic agent capable of inactivating the NS3 protein or is a serine **protease** inhibitor, an NTPase inhibitor or a helicase inhibitor.

L34 ANSWER 12 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-343953 [36] WPIDS
DNC C2001-106553
TI **Chimeric** live, infectious, attenuated yellow fever viruses used for preventing and treating diseases caused by flaviviruses have prM-E **nucleotide** sequence from a second, different flavivirus as functional yellow fever prM-E is not expressed.
DC B04 D16
IN CHAMBERS, T J; GUIRAKHOO, F; MONATH, T P
PA (ORAV-N) ORAVAX INC
CYC 93
PI WO 2001039802 A1 20010607 (200136)* EN 232p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001018139 A 20010612 (200154)
ADT WO 2001039802 A1 WO 2000-US32821 20001201; AU 2001018139 A AU 2001-18139 20001201
FDT AU 2001018139 A Based on WO 200139802
PRAI US 1999-452638 19991201
AB WO 200139802 A UPAB: 20010628
NOVELTY - **Chimeric** live, infectious, attenuated virus comprising a yellow fever virus with the **nucleotide** sequence encoding a prM-E protein deleted, truncated or mutated so that functional yellow fever virus prM-E protein is not expressed and also integrated into the genome of the yellow fever virus a **nucleotide** sequence (I) encoding a prM-E protein of a second, different flavivirus so that the prM-E protein of the second flavivirus is expressed.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a **nucleic acid** molecule encoding a **chimeric** live, infectious, attenuated virus comprising a yellow fever virus with the **nucleotide** sequence encoding a prM-E protein deleted, truncated or mutated so that functional yellow fever

virus prM-E protein is not expressed and also integrated into the genome of the yellow fever virus a **nucleotide** sequence (I) encoding a prM-E protein of a second, different flavivirus so that the prM-E protein of the second flavivirus is expressed; and

(2) use of a yellow fever virus vector comprising a gene encoding a gene product for preparing a medicament for producing the gene product in a cell of the patient.

ACTIVITY - Virucide.

YF/JE SA14-14-2 RMS and YF 17D viruses were inoculated by the subcutaneous route into groups of 8 mice. After 28 days surviving mice were challenged by intraperitoneal inoculation of 158 LD50 (2000 plaque forming units (PFU)) of JE virus (JaOArS982, IC37) and animals were observed for a following 21 days. The YF 17D virus gave minimal cross-protection against the JE challenge and the YF/JE SA14-14-2 RMS **chimera** was protective at doses at least 103 PFU.

MECHANISM OF ACTION - Vaccine.

USE - The **chimeric** live, infectious, attenuated virus is used to prepare medicaments for preventing or treating flavivirus infection in a patient (claimed). The yellow fever virus vector produces its gene product (tumor antigen or cytokine) in cells of the lymphoid or reticuloendothelial system or in a precursor of these systems in patients with cancer (claimed).

ADVANTAGE - Flaviviruses replicate in the cytoplasm of cells so that the virus replication does not involve integration of the **viral genome** into the host cell.

Dwg.0/32

TECH UPTX: 20010628

TECHNOLOGY FOCUS - BIOLOGY - Preferred Virus: The second flavivirus is a Japanese Encephalitis (JE) virus, a Dengue type 1, 2, 3 or 4 virus, a Murray Valley Encephalitis virus (i.e., Central European or Russian Spring-Summer Encephalitis virus), a Hepatitis C virus, a Kunjin virus, a Powassan virus, a Kyasanur Forest Disease virus and an Omsk Hemorrhagic Fever virus. Preferably the second flavivirus is a Dengue virus and the **nucleotide** sequences used are derived from two different strains. The prM signal of the **chimeric** virus is that of the yellow fever virus. The NS2B-NS3 **protease** recognition site and the signal sequences and cleavage sites at the C/prM and E/NS1 junctions are maintained in construction of the **chimeric** flavivirus.

Preferred **Nucleotide** Sequence: (I) replaces the **nucleotide** sequence encoding the prM-E protein of the yellow fever virus or comprises a mutation which prevents prM cleavage to produce M protein.

L34 ANSWER 13 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-227548 [24] WPIDS
DNC C2001-068092
TI Recombinant RNA comprising heterologous gene in Coxsackie **viral genome**, useful in gene therapy, specifically for targeting of cardiac myocytes.
DC B04 D16
IN KANDOLF, R; KUEPPER, J; MEYER, R; MEYER-FICCA, M
PA (UYTU-N) UNIV TUEBINGEN EBERHARD-KARLS
CYC 23
PI DE 19939095 A1 20010222 (200124)* 12p
WO 2001012815 A1 20010222 (200124) DE
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 2000062816 A 20010313 (200134)
EP 1210439 A1 20020605 (200238) DE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT DE 19939095 A1 DE 1999-19939095 19990818; WO 2001012815 A1 WO 2000-EP7768 20000810; AU 2000062816 A AU 2000-62816 20000810; EP 1210439 A1 EP 2000-949478 20000810, WO 2000-EP7768 20000810

FDT AU 2000062816 A Based on WO 200112815; EP 1210439 A1 Based on WO 200112815

PRAI DE 1999-19939095 19990818

AB DE 19939095 A UPAB: 20010502

NOVELTY - Recombinant RNA molecule (I), at least partly translatable in a target cell, comprises:

(a) the non-infectious genome (A) of Group B Coxsackie virus (CVB), particularly serotype B3; and

(b) at least one foreign gene (II) that can be developed for a selected function in the target cell, e.g. for gene therapy.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a recombinant infectious virions (V), derived from (A) and containing (I);

(2) a plasmid vector containing the **DNA** sequence (III) for (I), under control of a promoter;

(3) a helper construct for complementing the coding sequence exchanged by (I);

(4) producing (V);

(5) producing the plasmids of (2);

(6) producing helper constructs of (3);

(7) a kit containing the vector of (2) or the helper construct of (3);

(8) a **DNA** molecule (IV) containing at least one coding sequence for (I);

(9) a kit containing (IV);

(10) a kit for performing methods (5) or (6);

(11) a **DNA** construct that encodes (I) and can persist (and is transcribed) in target cells, but is preferably not replicable;

(12) a recombinant virus (RV), particularly adeno or retro, that encodes (I) and is expressed after infection into a target cell to produce a cytoplasmic replicon that is continuously replenished;

(13) producing recombinant **DNA** viruses or virions having a **DNA** genome that lacks a specific gene function, in which this function is provided from a recombinant vector system with a RNA genome.

ACTIVITY - Cardioactive.

MECHANISM OF ACTION - Gene therapy.

USE - (I) Is used to produce gene therapy vectors, particularly plasmids or virions, and these vectors are used for specific transfer to cardiac muscle, for diagnosis, prevention or treatment of cardiac disease, either congenital or acquired.

(I) Are also used to complement vectors that lack particular gene sequences, particularly vectors derived from **DNA** viruses.

ADVANTAGE - Vectors based on (I) transfer genes to cardiac myocytes without immunological or other side effects. The RNA genome can replicate, providing efficient gene transfer and long-term expression of the therapeutic gene. CBV is naturally trophic for heart muscle and since it does not produce **DNA** during its life cycle, overcomes the danger that foreign genes will become integrated in the target cell genome. By using (II) to replace part of the viral coding region, large (II) sequences may be accommodated. (I) is easily packaged in CVB capsid proteins.

Dwg.0/5

TECH UPTX: 20010502

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred materials: (I) is competent for replication in a target cell and in the **viral genome** component, parts of the coding sequence have been exchanged for at least one (II). Particularly the viral sequences exchanged are those that encode

any of capsid proteins VP1-VP4; **proteases** 2A and/or 3C (or these have been modified to eliminate cytotoxic effects on the target cell); helicase 2C and/or protein 2B.
Preferred virions of (1) correspond, as regards structural proteins to CVB.
The helper construct is:
(i) a plasmid or viral vector, encoding at least one of the exchanged functions; or
(ii) a helper cell, stably **transfected** with **DNA** encoding at least one of these functions.
Preferred method: To introduce (II) in a target cell. (I) is introduced by **transfection** or (V) by infection.
Preparation: (V) are prepared by **transfecting** a host cell with the plasmid of (2), then complementation of the exchanged sequence with the helper construct. Particularly the host cell is a helper cell. To produce the plasmid of (2), cDNA of CVB is cloned into a plasmid, then segments of the plasmid amplified, using primers, to produce amplicons that encode a non-infectious **viral genome**. These amplicons are then ligated to (II). Helper constructs are prepared similarly but the primers used amplify the region encoding the exchanged function. The specification lists suitable primers.
Preferred kits: The kits of (10) contain a plasmid with cloned cDNA for infectious CVB and suitable primers.

L34 ANSWER 14 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-112219 [12] WPIDS
CR 2001-080683 [09]
DNN N2001-082421 DNC C2001-033293
TI Expressing and isolating recombinant protein in a plant, useful for producing large quantities of recombinant proteins, by expressing a **fusion** protein including a cellulose binding peptide fused to a recombinant protein.
DC B04 C06 D16 P13
IN SHANI, Z; SHOSEYOV, O
PA (CBDT-N) CBD TECHNOLOGIES LTD; (YISS) YISSUM RES DEV CO HEBREW UNIV JERUSALEM; (YISS) YISSUM RES & DEV CO
CYC 94
PI WO 2000077174 A1 20001221 (200112)* EN 87p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000049475 A 20010102 (200121)
EP 1185624 A1 20020313 (200225) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003502032 W 20030121 (200308) 114p
ADT WO 2000077174 A1 WO 2000-IL330 20000607; AU 2000049475 A AU 2000-49475 20000607; EP 1185624 A1 EP 2000-931527 20000607, WO 2000-IL330 20000607; JP 2003502032 W WO 2000-IL330 20000607, JP 2001-503619 20000607
FDT AU 2000049475 A Based on WO 200077174; EP 1185624 A1 Based on WO 200077174; JP 2003502032 W Based on WO 200077174
PRAI US 1999-329234 19990610
AB WO 200077174 A UPAB: 20030204
NOVELTY - Expressing and isolating a recombinant protein in a plant, comprising expressing a **fusion** protein including the recombinant protein and a cellulose binding peptide fused to it, where the **fusion** protein is compartmentalized and sequestered within plant

cells, plant derived tissue or cultured plant cells, is new.

DETAILED DESCRIPTION - Expressing and isolating a recombinant protein in a plant, comprising expressing a **fusion** protein including the recombinant protein and a cellulose binding peptide fused to it, where the **fusion** protein is compartmentalized and sequestered within plant cells, plant derived tissue or cultured plant cells, is new. The method comprising:

(a) providing a plant, a plant derived tissue or cultured plant cells expressing a **fusion** protein including the recombinant protein and a cellulose binding peptide fused to it, the **fusion** protein is compartmentalized within plant cells, plant derived tissue or cultured plant cells, to be sequestered from cell walls of the plant, plant derived tissue or cultured plant cells;

(b) homogenizing the plant, plant derived tissue or cultured plant cells, to contact the **fusion** protein with plant derived cellulosic matter, plant derived tissue or cultured plant cells, to effect affinity binding of the **fusion** protein via the cellulose binding peptide to the cellulosic matter; and

(c) isolating the **fusion** protein cellulosic matter complex.

INDEPENDENT CLAIMS are also included for the following:

(1) a genetically modified or viral infected plant or cultured plant cells expressing a **fusion** protein including a recombinant protein and a cellulose binding peptide, where the **fusion** protein is compartmentalized within the plant cells;

(2) a composition of matter, comprising:

(a) a plant derived cellulosic matter; and

(b) a **fusion** protein including a recombinant protein and a cellulose binding peptide separated by a unique amino acid sequence which can be recognized and digested by a **protease** or under predetermined cis or trans conditions for digesting a controllable intervening protein sequence, where the **fusion** protein is expressed in the plant by affinity binding via the cellulose binding peptide;

(3) a nucleic acid molecule, comprising:

(a) a promoter sequence for directing protein expression in plant cells; and

(b) a heterologous nucleic acid sequence including:

(i) a sequence encoding a cellulose binding peptide;

(ii) a sequence encoding a recombinant protein, joined in frame to the sequence of (i); and

(iii) a sequence encoding a unique amino acid sequence which can be recognized and digested by a **protease** or under predetermined cis or trans conditions for digesting a controllable intervening protein sequence, the sequence is between and in frame with the sequences of (i) and (ii), and the heterologous nucleic acid sequence is down stream from the promoter sequence, so that expression of the heterologous nucleic acid is effected by the promoter sequence; and

(4) a nucleic acid molecule, comprising the sequence of (3), where (biii) encodes a **signal peptide** for directing a protein to a cellular compartment, the sequence being upstream and in frame with (i) and (ii).

USE - The method is useful for obtaining large quantities of the recombinant proteins and protein products in a simple and cost-effective manner. Recombinant proteins may be used commercially, such as in the food processing industry, e.g. glucoamylases and glucose isomerases are used for converting starch to high fructose corn syrup, proteinases for the hydrolysis of high molecular weight proteins and in manufacturing leather or alcoholic beverages, pectinesterases for pectin hydrolysis in food industry, lipases for cleaving ester linkage in triglycerides, and for effluent treatment. The recombinant proteins may further be used to

produce protein antibiotics, which can be used in healing processes, and to produce animal feed enzymes.

ADVANTAGE - The method provides a high level of expression of a recombinant protein and allows simple and effective recovery of the expressed recombinant protein without interference of the expressed products in the natural formation of the cell wall, which may result in growth arrest of the plant. Compared with previous methods, the new method allows a very high expression of the **fusion** protein and the specific activity of the **fusion** protein cellulosic matter complex formed, i.e. the number of **fusion** protein molecules per weight of cellulosic matter, is far superior.

Dwg.0/11

TECH UPTX: 20011227

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method further comprises washing the **fusion** protein cellulosic matter complex to remove endogenous plant proteins and other plant material, and collecting the **fusion** protein cellulosic matter complex as a final product of the process. The **fusion** protein cellulosic matter complex is then exposed to dissociating conditions, prior to isolating the **fusion** protein to obtain an isolated **fusion** protein. The dissociating conditions are basic conditions, denaturing conditions or affinity displacement conditions. The method further comprises digesting the **fusion** protein to release the recombinant protein. The digestion comprises proteolysis using a **protease** or under predetermined cis or trans conditions for digesting a controllable intervening protein sequence. The released recombinant protein is then isolated.

Preferred **Fusion** Protein: The **fusion** protein of the genetically modified or viral infected plant or culture plant cell is under the control of a constitutive or tissue specific plant promoter. The **fusion** protein is compartmentalized within, a cellular compartment selected from cytoplasm, endoplasmic reticulum, Golgi apparatus, oil bodies, starch bodies, chloroplasts, chromoplastids, chromoplasts, vacuole, lysosomes, mitochondria, or nucleus.

Preferred Nucleic Acid: The nucleic acid molecule further comprises a sequence element selected from an origin of replication for propagation in bacterial cells, at least one sequence element for integration into a plant's genome, a polyadenylation recognition sequence, a transcription termination signal, a sequence encoding a translation start site or stop site, plant RNA **virus** derived sequences, or a transposable element derived sequence. The heterologous nucleic acid sequence may further include a fourth sequence encoding a unique amino acid sequence which can be recognized and digested by **protease** or under predetermined cis or trans conditions for digesting a controllable intervening protein sequence. The fourth sequence is between and in frame with sequences (i) and (ii).

L34 ANSWER 15 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-080752 [09] WPIDS
DNC C2001-023297
TI **Chimeric** chemokine-antigen polypeptides which elicit enhanced immune responses and which may be used as vaccines, especially to vaccinate against human immuno deficiency **virus**-1.
DC B04 D16
IN GALLO, R C; GARZINO-DEMO, A; LIM, S P; TAN, Y H
PA (GALL-I) GALLO R C; (GARZ-I) GARZINO-DEMO A; (MOLE-N) INST MOLECULAR & CELL BIOLOGY; (LIMS-I) LIM S P; (TANY-I) TAN Y H; (UYMA-N) UNIV MARYLAND BIOTECHNOLOGY INST
CYC 93
PI WO 2000078334 A1 20001228 (200109)* EN 123p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000056179 A 20010109 (200122)

ADT WO 2000078334 A1 WO 2000-US16598 20000616; AU 2000056179 A AU 2000-56179 20000616

FDT AU 2000056179 A Based on WO 200078334

PRAI US 1999-335150 19990617

AB WO 200078334 A UPAB: 20010213

NOVELTY - **Chimeric** chemokine-antigen polypeptides (CHIMI), which elicit an enhanced immune response and which may be used as vaccines, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a **chimeric** polypeptide (polypep) (CHIMI), comprising:

(a) one or more chemokine polypeps (CP) selected from:

(i) chemokines; and

(ii) polypeptides within one or more of the following groups: chemokine fragments, chemokine analogs, chemokine derivatives and chemokine truncation isoforms;

(b) one or more antigenic polypeps (AG);

(c) one or more polypep linkers (PL) connecting the CPs to the APs;

(2) a polynucleotide (NUCI) comprising a nucleotide sequence encoding the **chimeric** polypep (CHIMI);

(3) an expression vector (VECI) comprising (NUCI);

(4) a host cell (CELLI) transformed by the expression vector (VECI) and which expresses (CHIMI);

(5) a live vector vaccine (VACCI) comprising (VECI);

(6) a method (METHI) for eliciting an immune response comprising administering (CHIMI) and/or (NUCI);

(7) compositions ((COMPI) and (COMPII)) comprising (CHIMI) or (NUCI) and a carrier;

(8) a method (METHII) of producing **chimeric** polypeps (i.e. (CHIMI), comprising:

(a) preparing an expression vector (i.e. (VECI)) comprising an nucleotide sequence (i.e. (NUCI)) encoding a **chimeric** polypep (i.e. (CHIMI));

(b) transforming a host cell (i.e. (CELLI)) with the vector; and

(c) causing the host cell to express the **chimeric** amino acid;

(9) a polypep (PEPI) comprising a sequence from one of 4 defined amino acid sequences ((A1)-(A4)) given in the specification (especially amino acids 25-477 of (A1), 17-493 of (A2), 23-477 of (A3) and 24-528 of (A4)); and

(10) a nucleotide (NUCI) encoding (PEPI).

ACTIVITY - Antiviral.

MECHANISM OF ACTION - Vaccine with improved immunological properties (claimed).

USE - The **chimeric** polypep (CHIMI) may be used as a vaccine to immunize a subject (preferably a human) against a variety of antigens derived from plants, fungi, protozoa, a bacteria pathogenic to humans and/or **viruses** (especially human immunodeficiency **virus** (HIV)-1. Alternatively, it may be a self-antigen, allergen or tumor associated antigen (claimed).

ADVANTAGE - Vaccine with improved immunological properties (claimed). Groups of 4 animals were injected with naked DNA as follows:

(1) 100 micro g DNA vector and no antigen (group A);

(2) 50 micro g of a construct encoding p24 and 50 micro g of a vector (group B);

(3) 50 micro g of a construct encoding p24 and 50 micro g of a construct encoding murine MCP-1 (pcmuMCP1) (group C); and

(4) 50 micro g of the construct pTORINO (encodes and expresses a **chimera** of MCP-1 and p24 (group D).

The mice were injected 3 times at weeks 0, 2 and 4 and the mice were bled prior to each injection. After the injections bleeding of the animal was performed every 2 weeks for a total of 8 bleedings. To date, results have been obtained for bleed 1 (prior to immunization i.e. preimmune sera) and a bleed 4 (2 weeks after the last injection). It was found that the use of the chimeric construct enhanced the immune response 2-fold. At an optical density of 450 nm:

(1) group A had an antibody titer of 0.936;

(2) group B had an antibody titer of 1.040;

(3) group C had an antibody titer of 1.258; and

(4) group D had an antibody titer of 1.988.

Dwg.0/0

TECH UPTX: 20010213

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polypeptides: In (CHIMI) at least one or more of the PLs connect one or more APs to one or more of the CPs in a manner that does not eliminate the antigenicity of the AP and which does not eliminate the biological activity of the CP. One or more of the PLs comprises 2-30 (especially 5-28) amino acids. At least 1 region of the PLs comprises all or a portion of an antibody hinge region having 50-100 (especially 90-100)% sequence homology to a naturally occurring antibody hinge region. The antibody hinge region is selected from the hinge regions of the heavy chains of immunoglobulin (Ig) G2a and IgG2b. At least 1 of the PLs is selected from a series of 33 defined amino acid sequences given in the specification (e.g. Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser and Ala-Gly-Ser-Ala-Gly-Ser-Ala-Gly-Ser-Ala-Gly-Ser). At least one of the linkers comprises the sequence Glu-Pro-Arg-Val-Pro-Ile-Thr-Gln-Asn-Pro-Cys-Pro-Pro.

(CHIMI) Further comprises a **signal peptide** which is cleavable from the **chimeric** polypeptide by enzymatic cleavage.

One or more of the APs is derived from a plant, fungi, protozoa, a bacteria pathogenic to humans and/or **viruses**. Alternatively, it may be a self-antigen, allergen or tumor associated antigen. Preferably the AP includes one or more Human Immunodeficiency **Virus** (HIV) antigens selected from gag p55, gag p17, gag p5, gag p65, HIV **protease** reverse transcriptase, gp120, gp160, gp41, tat, rev, nef, vpu and/or vif. In particular, the HIV antigen includes HIV-1 p24 strain IIB.

The CP is selected from a chemokine of class C, CXC, C-C and/or CX3C. The CP is preferably selected from: macrophage derived chemokine, monocytes chemotactic protein (MCP) 1, MCP 2, MCP 3, MCP 4, activated macrophage specific chemokine 1, macrophage inflammatory protein (MIP) 1 alpha, MIP 1 beta, MIP 1 gamma, MIP 1 delta, MIP 2 alpha, MIP 3 alpha, MIP 3 beta, regulated upon activation, normal T cell expressed and secreted (and its variants), I-309, EBI1-ligand chemokine, pulmonary and activation regulated chemokine, liver and activation-regulated chemokine, thymus and activation regulated chemokine, Eotaxin (and variants), human CC chemokine (HCC) 1, HCC 2, HCC 3, interleukin-10-inducible chemokine, liver and activation-regulated chemokine, thymus-expressed chemokine, secondary Lymphoid tissue chemokine, lymphocyte and monocyte chemoattractant, Monotactin, activation induced , chemokine-related molecule, myeloid progenitor inhibitory factor (MPIF) 1, MPIF 2, stromal cell-derived factor (SCDF) 1 alpha, SCDF 1 beta, B-cell-attracting chemokine 1, HuMIG, H174, interferon-stimulated T-cell alpha chemoattractant, interleukin-8, IP-10, platelet factor 4, growth-regulated-gene (GRG) alpha, GRG beta, GRG gamma,

neutrophil-activating protein 2, ENA-78, granulocyte chemotactic protein 2, lymphotactin, Fractalkine/neutrotactin, viral chemokines, and functional equivalents of them.
(CHIMI) Is chemotactic for one or more cells selected from dendritic cells, monocytes, macrophages, B-cells and T-cells.
The CP is selected from MDC, BLC, RANTES, MCP-1 and functional equivalents. The CP comprises a derivative of a chemokine having one or more insertions or substitutions with one or more non-classical amino acids, and the derivative has the ability to enhance an immune response. Preferably, the CP comprises a derivative of a chemokine having at least one conservative substitution in the amino acid sequence and the derivative has the ability to enhance the immune response. The CP comprises a human chemokine. The CP preferably comprises one of 4 defined amino acid sequences ((A1)-(A4)) given in the specification, especially amino acids 25-477 of (A1), 17-493 of (A2), 23-477 of (A3) and 24-528 of (A4).
(CHIMI) Preferably has the formula:
C-L-A
C = a CP comprising either a chemokine or a chemokine fragment, chemokine analogue, chemokine derivative or chemokine truncation isoform;
A = an AP; and
L = a PL which does not eliminate the biological activity of C or the antigenicity of A.
C, L and A are joined by peptide bonds.
Preferred Polynucleotides: (NUCI) comprises one of 4 defined nucleotide sequences given in the specification.
Preferred Methods: IN (METHI) the immune response is enhanced relative to an immune response in a corresponding subject to whom a corresponding antigen is administered either alone or attached to a non-chemokine polypep. The subject is preferably a human infected (or at risk of being infected) with HIV **virus**. The immune response is a humoral response and/or a cell-mediated response.
Preferred Compositions: (COMPI) and (COMPII) are formulated for administration as a vaccine. The carrier is a physiological buffer, a physiological saline, buffered saline, a slow release carrier, an emulsion, and a liposome preparation. The compositions may further comprise excipients, auxiliary substances, adjuvants, wetting or emulsifying agents and pH buffering agents.
Preparation: (CHIMI) may be produced according to standard recombinant DNA methodologies (e.g. by culturing (CELLI).

L34 ANSWER 16 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-080683 [09] WPIDS
CR 2001-112219 [05]
DNC C2001-023259
TI Expressing and isolating recombinant protein from plant e.g for use in food industry, involves homogenizing a plant expressing **fusion** protein including recombinant protein and cellulose binding peptide being fused to it.
DC B04 C06 D16
IN SHANI, Z; SHOSEYOV, O
PA (CBDT-N) CBD TECHNOLOGIES LTD; (FRIE-I) FRIEDMAN M M; (YISS) YISSUM RES & DEV CO
CYC 90
PI WO 2000077175 A1 20001221 (200109)* EN 64p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL

TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000051369 A 20010102 (200121)
US 6331416 B1 20011218 (200205)
ADT WO 2000077175 A1 WO 2000-US13434 20000517; AU 2000051369 A AU 2000-51369 20000517; US 6331416 B1 US 1999-329234 19990610
FDT AU 2000051369 A Based on WO 200077175
PRAI US 1999-329234 19990610
AB WO 200077175 A UPAB: 20020123
NOVELTY - A plant, a plant derived tissue or cultured plant cells expressing a **fusion** protein (FP) including a recombinant protein (RP) and a cellulose binding peptide (CBP) being fused to it, is homogenized so that FP is contacted with a plant derived cellulosic matter, which effects affinity binding of FP via CBP to the cellulosic matter (CM). A FP cellulosic matter complex is formed and isolated.

DETAILED DESCRIPTION - A process of expressing a recombinant protein in a plant and isolating the recombinant protein from the plant comprises:

(a) providing a plant, a plant derived tissue or cultured plant cells expressing FP including (RP) and CBP being fused to it, FP being compartmentalized so as to be sequestered from the cell walls;

(b) homogenizing the plant, plant derived tissue or cultured plant cells such that FP is brought into contact with a plant derived cellulosic matter CM to effect affinity binding of FP via CBP to CM and forming a FP-CM complex; and

(c) isolating the FP-CM complex.

INDEPENDENT CLAIMS are also included for the following:

(1) a genetically modified or viral infected plant (I) or cultured plant cells expressing FP including RP and CBP, FP being compartmentalized within cells of plant or cultured plant cells, so as to be sequestered from the cell walls of the plant cells or of the cultured plant cells. RP and CBP are separated through a unique amino acid sequence recognizable and digestible by a **protease** or under predetermined cis or trans conditions for digesting a controllable intervening protein sequence;

(2) a composition of matter (II) comprising:

(a) a plant derived CM of a plant; and

(b) FP including RP and CBP separated through a unique amino acid sequence recognizable and digestible by a **protease** or under predetermined cis or trans conditions for digesting a controllable intervening protein sequence, FP being expressed in the plant and complexed to the plant derived CM of the plant by affinity binding through CBP; and

(3) a nucleic acid molecule (III) comprising:

(a) a promoter sequence for directing protein expression in plant cells,

(b) a heterologous nucleic acid sequence including:

(i) a first sequence encoding CBP;

(ii) a second sequence encoding RP, where the first and second sequence are joined together in frame;

(iii) a third sequence encoding a **signal peptide** for directing a protein to a cellular compartment, the third sequence being upstream and in frame with the first and second sequences; and/or

(iv) a fourth sequence encoding a unique amino acid sequence being recognizable and digestible by a **protease** or under predetermined cis or trans conditions for digesting a controllable intervening protein sequence, the fourth sequence being between in frame with the first and second sequences;

where the heterologous nucleic acid sequence is downstream from the promoter sequence, such that expression of the heterologous nucleic acid sequence is effectable by the promoter sequence.

USE - RP isolated by this method is useful commercially in the food industry, for the hydrolysis of high molecular weight protein, in the

manufacture of alcoholic beverages, for the hydrolysis of whey lactose, in the production of the artificial sweetener aspartame, in the reduction of the cooked flavor of milk, in the production of animal feed enzymes, in the sterilization and oxidation of plastics and rubbers, for the production of heparin and heparan sulfate oligosaccharides, for purification in industrial processes, for production of protein fibers, for effluent treatment, in combination with detergents in cleaning applications, and in leather manufacturing processes.

ADVANTAGE - The method provides a plant expression system where a high level of expression is achievable and which allows simple and effective recovery of the expressed recombinant protein. The method exploits the high affinity between CBP and cellulose, the inherent abundance of cellulose in the plant, and the simplicity associated with cellulose isolation from the plant, plant derived tissue and/or cultured (P) cells and overcomes the shortcomings of conventional methods e.g. as the expressed protein is sequestered from the cell walls of the plant cells or of the cultured plant cells, there is no interference with the natural formation of the cell wall and consequently no arrested plant growth.

Dwg.0/1

TECH UPTX: 20010213

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method further comprises the steps of:

(a) washing the FP-CM complex to remove endogenous plant proteins and other plant material from it;

(b) collecting FP-CM complex as a final product of the process;

(c) exposing FP-CM complex to conditions effective in dissociating FP from CM, where the conditions are selected from basic conditions, denaturative conditions and affinity displacement conditions;

(d) isolating FP;

(e) exposing isolated FP to conditions effective in digesting FP so as to release RP, where the conditions are selected from proteolysis effected by a **protease** and proteolysis effected under predetermined cis or trans conditions for digesting a controllable intervening protein sequence;

(f) isolating RP; and

(g) exposing FP-CM complex to conditions effective in digesting FP so as to release RP, where the conditions are selected from proteolysis effected by a **protease** and proteolysis effected under predetermined cis or trans conditions for digesting a controllable intervening protein sequence.

Preferred Plant: The expression of FP is under the control of a constitutive or tissue specific plant promoter and FP is compartmentalized within a cellular compartment such as cytoplasm, endoplasmic reticulum, golgi apparatus, oil bodies, starch bodies, chloroplastids, chloroplasts, chromoplastids, chromoplasts, vacuole, lysosomes, mitochondria, or nucleus, (so as to be sequestered from the cell walls of the plant or cultured plant cells).

Preferred Nucleic Acid: (III) further comprises a sequence element selected from an origin of replication for propagation in bacterial cells, at least one sequence element for integration into a plant's genome, a polyadenylation recognition sequence, a transcription termination signal, a sequence encoding a translation start site, a sequence encoding a translation stop site, plant RNA **virus** derived sequences, plant DNA **virus** derived sequences, tumor inducing (Ti) plasmid derived sequences, and a transposable element derived sequence.

L34 ANSWER 17 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-071394 [08] WPIDS
DNN N2001-054019 DNC C2001-020031

TI New polynucleotides encoding scorpion venom potassium-channel agonist proteins for production e.g. of insect-tolerant transgenic plants for controlling insect pest damage and parasitic worm infections.
DC B04 C05 C06 D16 S03
IN HERRMANN, R; LEE, J; WONG, J F; HERMANN, R
PA (DUPO) DU PONT DE NEMOURS & CO E I; (HERM-I) HERMANN R; (WONG-I) WONG J F
CYC 90
PI WO 2000078958 A2 20001228 (200108)* EN 50p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 2000057543 A 20010109 (200122)
EP 1185654 A2 20020313 (200225) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002160454 A1 20021031 (200274)
ADT WO 2000078958 A2 WO 2000-US17049 20000621; AU 2000057543 A AU 2000-57543 20000621; EP 1185654 A2 EP 2000-943006 20000621, WO 2000-US17049 20000621; US 2002160454 A1 Provisional US 1999-140227P 19990622, Cont of US 2000-599416 20000622, US 2002-44359 20020111
FDT AU 2000057543 A Based on WO 200078958; EP 1185654 A2 Based on WO 200078958
PRAI US 1999-140227P 19990622; US 2000-599416 20000622; US 2002-44359 20020111
AB WO 200078958 A UPAB: 20010207
NOVELTY - An isolated polynucleotide (I) comprising a nucleotide sequence selected from a nucleotide sequence (III) of at least 81 nucleotides selected from 10 sequences of 171-213 nucleotides (N1)-(N10), a nucleotide sequence (III) encoding a polypeptide of at least 27 amino acids selected from 10 sequences of 56-70 amino acids (P1)-(P10), or a complement of (III) or (IV), is new.

DETAILED DESCRIPTION - An isolated polynucleotide (I) encoding a potassium-channel (K-channel) agonist comprises: (a) a nucleotide sequence selected from a nucleotide sequence (III) of at least 81 nucleotides selected from (N1)-(N10); (b) a nucleotide sequence (IV) encoding a polypeptide of at least 27 amino acids that has at least 80% identity based on the Clustal method of alignment when compared to a polypeptide selected from (P1)-(P10); and/or (c) a complement of (III) or (IV);

(N1)-(N10) comprise nucleotide sequences encoding ten respective scorpion venom K-channel agonist proteins and their **signal peptides** (sequences (P1)-(P10) respectively); all sequences being given in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) a **chimeric** gene/(vector) (II) comprising (I) operably linked to at least one suitable regulatory sequence;

(2) a host cell comprising (I) or (II);

(3) a **virus** comprising (I);

(4) a polypeptide of at least 27 amino acids that has at least 80% identity based on the Clustal method of alignment when compared to a polypeptide selected from (P1)-(P10);

(5) a method of obtaining a nucleic acid fragment encoding a K-channel agonist comprising:

(a) synthesizing an oligonucleotide primer (V) comprising a nucleotide sequence of at least 30 contiguous nucleotides derived from a nucleotide sequence selected from (N1)-(N10) and their complements; and amplifying a nucleic acid sequence using (V); or

(b) probing a **cDNA** or genomic **library** with an isolated polynucleotide (VI) comprising a nucleotide sequence of at least

30 contiguous nucleotides derived from a nucleotide sequence selected from (N1-N10) and their complements; identifying a DNA clone that hybridizes with (VI); isolating the clone; and sequencing a cDNA or genomic fragment that comprises the isolated DNA;

(6) a recombinant baculovirus expression vector comprising a DNA sequence encoding a polypeptide of at least 27 amino acids selected from (P1)-(P10); and

(7) A method for testing the activity of a K-channel agonist against insects comprising (a) amplifying a nucleic acid sequence; (b) using restriction enzyme analysis to confirm that the required nucleic acid fragment is present; (c) isolating the nucleic acid fragment; (d) propagating colonies containing the isolated nucleic acid fragment; (e) co-transfecting the isolated nucleic acid fragment into host cells with linearized polyhedron-negative baculovirus; (f) feeding larvae a viral-contaminated diet; and (g) comparing a reaction of a viral-contaminated larvae to that of a non-contaminated control group.

ACTIVITY - Antiparasitic; Antihelmintic; Insecticide.

Ten complementary DNA (cDNA) clones of the sequences (N1)-(N10) encoding the scorpion potassium-channel (K-channel) modifier proteins described in the sequences (P1)-(P10) respectively, were each cloned into the baculovirus transfer vector pAcUW21 (BD Biosciences-PharMingen, San Diego, CA). This plasmid DNA was used for lipofectin-mediated co-transfection with linearized polyhedron negative AcNPV, into insect cells. Polyhedron-positive recombinant **viruses** were isolated and mixed with a plug of HV diet (www.Bio-Serv.com) and fed to larvae of the lepidopteran Heliothis virescens. Four 5 day-old larvae were fed 200 mg of viral contaminated diet. The larvae were allowed to eat for 2 days or until the viral-contaminated diet was consumed, then fresh 1 g diet plugs were added to allow continued feeding. Results showed that 4-7 days after the fresh diet was added, the majority of the larvae had low diet consumption and retardation in growth. In summary, the K-channel modifier peptides encoded by the scorpion sequences (N1)-(N10), depicted in the peptide sequences (P1)-(P10) respectively, showed toxic activity against the lepidopteran Heliothis virescens.

MECHANISM OF ACTION - Potassium channel agonist.

No suitable data given.

USE - For the creation of transgenic plants which express K-channel modifiers, useful as a means for controlling insect pests by producing insect-tolerant plants. In the prevention and/or treatment of insect pest damage and parasitic worm infections in animals and humans, the invention may also find use in creating specific new pesticides and antihelmintic drugs that are also non-toxic to humans, pets and livestock.

ADVANTAGE - Insecticidal baculoviruses provide an environmentally benign method for agricultural pest control, especially in the production of transgenic plants that are more insect-tolerant than the naturally occurring variety.

Dwg.0/8

TECH UPTX: 20010207

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Nucleic Acid: (I) is DNA or RNA, comprising a sequence having at least 30 contiguous nucleotides, which encodes a mature scorpion K-channel agonist protein (preferably an arthropod K-channel blocking toxin 15-1, Bmtx toxin, neurotoxin P2, leiurotoxin I, leiuropeptide I, leiuropeptide III, kaliotoxin 1 precursor, or cobatoxin 1 polypeptide).

Preferred Host Cell: The host cell is a yeast, bacterial, plant, mammalian or insect cell.

L34 ANSWER 18 OF 35 WPIDS (C) 2003 THOMSON DERWENT

AN 2000-687336 [67] WPIDS

DNC C2000-209225

TI Using vectors encoding angiogenic factors for treatment or prevention of pulmonary arterial hypertension.

DC B04 D16

IN ADNOT, S; BRANELLEC, D

PA (AVET) AVENTIS PHARMA SA; (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (ADNO-I) ADNOT S; (BRAN-I) BRANELLEC D

CYC 93

PI WO 2000065043 A1 20001102 (200067)* FR 35p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2792531 A1 20001027 (200067)
AU 2000043017 A 20001110 (200109)
BR 2000010034 A 20020115 (200214)
EP 1173564 A1 20020123 (200214) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CZ 2001003813 A3 20020213 (200221)
NO 2001005223 A 20011025 (200221)
KR 2002001846 A 20020109 (200246)
US 2002086004 A1 20020704 (200247)
HU 2002000961 A2 20020729 (200258)

ADT WO 2000065043 A1 WO 2000-FR1060 20000421; FR 2792531 A1 FR 1999-5272 19990426; AU 2000043017 A AU 2000-43017 20000421; BR 2000010034 A BR 2000-10034 20000421, WO 2000-FR1060 20000421; EP 1173564 A1 EP 2000-922713 20000421, WO 2000-FR1060 20000421; CZ 2001003813 A3 WO 2000-FR1060 20000421, CZ 2001-3813 20000421; NO 2001005223 A WO 2000-FR1060 20000421, NO 2001-5223 20011025; KR 2002001846 A WO 2000-FR1060 20000421, KR 2001-713633 20011024; US 2002086004 A1 Provisional US 1999-139734P 19990618, Cont of WO 2000-FR1060 20000421, US 2001-983885 20011026; HU 2002000961 A2 WO 2000-FR1060 20000421, HU 2002-961 20000421

FDT AU 2000043017 A Based on WO 200065043; BR 2000010034 A Based on WO 200065043; EP 1173564 A1 Based on WO 200065043; CZ 2001003813 A3 Based on WO 200065043; KR 2002001846 A Based on WO 200065043; HU 2002000961 A2 Based on WO 200065043

PRAI US 1999-139734P 19990618; FR 1999-5272 19990426

AB WO 200065043 A UPAB: 20001223

NOVELTY - Use of a vector (A), containing a **nucleic acid** (I) that encodes an angiogenic factor (II), to prepare a composition for prevention, alleviation and/or treatment of pulmonary arterial hypertension (PAH), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing a composition for preventing, alleviating and/or treating PAH by combining (A) with one or more adjuvants; and

(2) a pharmaceutical composition comprising a defective recombinant virus that contains (I) in a formulation for intratracheal administration.

ACTIVITY - Angiogenic; antihypertensive.

When vascular endothelial growth factor was expressed from a recombinant adenovirus in the lungs of a rat that had been subjected to hypoxia, the treated animals showed significantly lower pulmonary arterial pressure and left ventricular hypertrophy than untreated controls.

MECHANISM OF ACTION - Angiogenesis.

USE - (A) are used to treat PAH.

ADVANTAGE - Treatment with (II) reduces pulmonary arterial pressure and prevents left ventricular hypertrophy and remodeling of the pulmonary vasculature that are associated with PAH more effectively than any known

method.

DESCRIPTION OF DRAWING(S) - Map of the plasmid pXL3264 used to produce a recombinant adenovirus that expresses a fusion protein of fibroblast growth factor-1 and the **signal peptide** of beta -interferon.

Dwg.1/3

TECH UPTX: 20001223

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: (I) encodes an angiogenic factor for epithelial cells, i.e. fibroblast growth factor (FGF) or vascular endothelial growth factor (VEGF), especially FGF-1, -2, -4 or -5, or VEGF-B or -C, or their variants, preferably including the sequence for a **signal peptide**.

Preferred Vectors: These are either plasmids, cosmids or any **DNA** not packaged in a virus or recombinant viruses, preferably adeno, retro, herpes or adeno-associated, especially a defective recombinant adenovirus of human types 2 or 5. Especially the adenovirus lacks at least the E1a and E1b regions, optionally also E4, and (I) replaces one of these deletions or is inserted at any other position in the **viral genome**, other than in a sequence required in cis for production of virus. For administration, the virus may be combined with a transfection auxiliary, e.g. a cationic lipid.

L34 ANSWER 19 OF 35 WPIDS (C) 2003 THOMSON DERWENT

AN 2000-593715 [56] WPIDS

DNN N2000-439662 DNC C2000-177288

TI Producing transgenic Impatiens plants for obtaining plants, seeds or progenies with enhanced resistance environmental stresses and commercial value by introducing an expression vector having a selectable marker and a foreign gene.

DC C06 D16 P13

IN CHOU, T

PA (BALL-N) BALL HORTICULTURAL CO

CYC 1

PI US 6121511 A 20000919 (200056)* 12p

ADT US 6121511 A Provisional US 1997-58902P 19970912, US 1998-151782 19980911

PRAI US 1997-58902P 19970912; US 1998-151782 19980911

AB US 6121511 A UPAB: 20001106

NOVELTY - Producing transgenic Impatiens plants by introducing expression vectors comprising a selectable marker gene and foreign gene, into a plant tissue explant using Agrobacterium, culturing the explant on selection medium and on regeneration medium, and recovering the fertile transgenic plants from the explants capable of transmitting foreign gene to progeny, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) fertile transgenic Impatiens plants produced by the novel method; and

(2) seeds and progeny of the transgenic Impatiens plant of (1).

USE - The method is useful for obtaining transgenic Impatiens plants that express at least one macromolecule, which confers resistance to environmental stresses and with enhanced commercial value. The method is also useful for transforming Impatiens plants with enhanced viral resistance, drought resistance and imparts fragrance as well.

Dwg.0/1

TECH UPTX: 20001106

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The Impatiens plant tissue explant obtained from shoot tips, hypocotyl tips or node regions. Prior to introduction of the expression vector to the explant, the explant is pre-cultured for 5 days in Murashige and Skoog (MS) medium containing approximately 0.5-2 mg/l 1-phenyl-3-9,(2,3-thiadiazol-5-yl)urea (TDZ), and

then subcultured in MS medium containing auxin, preferably 0.05-0.2 mg/l 1-naphthylacetic acid (NAA), and cytokinin, preferably 1-6 mg/l zeatin for about 48 hours. The selectable gene marker system is the nptII gene. The plant tissue explant is transferred to a selection medium, which is an MS medium comprising auxin and cytokinin with 500 mg/l carbenicillin, 100 mg/ml kanamycin, and 100 mg/ml cefotaxmine. The regeneration medium is the same as the selection medium.
Preferred Vector: The expression vector comprising the second foreign gene further comprises a promoter which may be a cauliflower mosaic virus (CaMV) 35S promoter, an enhanced 35S promoter, a UBQ3, UBQ10, UBQ11 or UBQ14 promoter, TEFA 1 promoter, ro1C promoter, or the Commelina yellow mottle virus promoter, preferably CaMV 35S promoter, where expression of the second foreign gene is under the control of the promoter. The expression vector may further comprise a third foreign gene encoding a beta-1,3-glucanase, while the second foreign gene encodes a chitinase.
Preferred Foreign Gene: The foreign gene confers resistance to disease-causing pathogens such as virus, bacterium, fungus and insect. The foreign gene that confers resistance to a virus disrupts viral function, and this virus-disrupting gene comprises a viral coat protein, a 2'-5' **oligonucleotide** synthetase, a **viral genome** antisense RNA or a pokeweed antiviral protein. The insect resistance gene may be a tryptophan decarboxylase, a lectin, particularly Galanthus nivalis lectin, or a Bacillus thuringiensis toxin. The second foreign gene that confers resistance to a bacterium or a fungus encodes a chitinase, a beta-1,2-glucanase, a ribosome-inactivating protein, a lytic peptide or the plant defensin radish seed Rs-AFP2. The second foreign gene is operatively linked with a **DNA** molecule encoding pea vicilin **signal peptide**. Alternatively, the expression of the second foreign gene confers insensitivity to ethylene, where this gene encodes a mutated ethylene receptor. The mutated ethylene receptor gene is the Arabidopsis etr-1 gene or a tomato NR gene. The second foreign gene may also be a Vitreoscilla hemoglobin gene, or an isopentenyl transferase gene, where its expression is under the control of the Arabidopsis SAG12 gene promoter of a senescence-associated gene. The second foreign gene selected from the following genes: PLENA, SQUAMOSA, DEFICIENS A, GLOBOSA, APTELA1, APETALA3, AGAMOUS, OsMADS24, OsMADS45 or the OsMADS1 gene, encodes a polypeptide having a MADS box domain. The second foreign gene may also encode a protein that modifies plant habit; resistance to Impatience necrotic spot virus (INSV), where it encodes INSV S, M and L RNAs; resistance to tomato spotted wilt virus (TS WV), where it encodes TSWV viral movement protein; fragrance, where the gene is a linalool or a limonene synthase gene; or resistance to drought, salinity or cold, where the gene is an Escherichia coli MnSOD gene, asparagine synthetase gene or promoter, Delta1-pyrroline-5-carboxylate synthetase gene, bacterial fructan gene, CAP85 or CAP160 genes, or trg-31.

L34 ANSWER 20 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-452408 [39] WPIDS
CR 2002-154752 [20]
DNC C2000-137957
TI New **nucleic acid** molecule encoding an **alphavirus** capsid, a **signal peptide**, and an **alphavirus** E1 or E2 glycoprotein, useful in the development of packaging systems for the high level production of recombinant **alphavirus** vector particles.
DC B04 D16
IN BELLI, B A; DUBENSKY, T W; HARDY, S F; POLO, J M; SILVIA, P; BELI, B; PERRI, S; POLO, J
PA (CHIR) CHIRON CORP
CYC 91

PI WO 2000039318 A1 20000706 (200039)* EN 94p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000022208 A 20000731 (200050)
US 6242259 B1 20010605 (200133)
EP 1141361 A1 20011010 (200167) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6329201 B1 20011211 (200204)
US 6423544 B1 20020723 (200254)

ADT WO 2000039318 A1 WO 1999-US31193 19991230; AU 2000022208 A AU 2000-22208 19991230; US 6242259 B1 Provisional US 1998-114732P 19981231, US 1999-476299 19991230; EP 1141361 A1 EP 1999-966715 19991230, WO 1999-US31193 19991230; US 6329201 B1 Provisional US 1998-114732P 19981231, CIP of US 1999-476299 19991230, US 2000-609154 20000630; US 6423544 B1 Provisional US 1998-114732P 19981231, CIP of US 1999-476299 19991230, US 2000-608730 20000630

FDT AU 2000022208 A Based on WO 200039318; EP 1141361 A1 Based on WO 200039318; US 6329201 B1 CIP of US 6242259; US 6423544 B1 CIP of US 6242259

PRAI US 1998-114732P 19981231; US 1999-476299 19991230; US 2000-609154 20000630; US 2000-608730 20000630

AB WO 200039318 A UPAB: 20020829
NOVELTY - A new **nucleic acid** molecule (N1) comprising a **nucleic acid** sequence which encodes, in order, an **alphavirus** capsid, a **signal peptide**, and an **alphavirus** E1 or E2 glycoprotein, providing that the **nucleic acid** molecule does not encode an **alphavirus** E2 or E1 glycoprotein, respectively.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an expression cassette, comprising a promoter and N1, where the promoter is operably linked to and directs the expression of the **nucleic acid** molecule;

(2) an expression cassette, comprising a promoter and a **nucleic acid** molecule which encodes a **signal peptide** and **alphavirus** glycoprotein E1, where the promoter is operably linked to and directs the expression of the **nucleic acid** molecule, and where the **nucleic acid** molecule does not encode an **alphavirus** E2 glycoprotein;

(3) an expression cassette, comprising a 5' sequence which initiates transcription of **alphavirus** RNA, an **alphavirus** subgenomic junction region promoter, N1 and a 3' **alphavirus** replicase recognition sequence;

(4) a host cell, comprising the expression cassette of (1), (2) or (3);

(5) an **alphavirus** packaging cell, comprising:

(a) a first expression cassette which directs the expression of a first **nucleic acid** molecule, comprising a **nucleic acid** sequence which encodes, in order, an **alphavirus** capsid, a **signal peptide**, and an **alphavirus** E1 glycoprotein, providing that the first **nucleic acid** molecule does not encode an **alphavirus** E2 glycoprotein; and

(b) a second expression cassette which directs the expression of a second **nucleic acid** molecule, comprising a

nucleic acid sequence which encodes, in order, an **alphavirus** capsid, a **signal peptide**, and an **alphavirus** E2 glycoprotein, providing that the second **nucleic acid** molecule does not encode an **alphavirus** E1 glycoprotein;

(6) a method of producing **alphavirus** vector particles, comprising introducing a vector selected from **alphavirus** vector constructs, RNA vector replicons, eukaryotic layered vector initiation systems, or **alphavirus** vector particles, into the packaging cell line of (5);

(7) an expression cassette (EC1), comprising a promoter which is operably linked to a **nucleic acid** molecule, which when transcribed produces an RNA sequence complementary to an **alphavirus** junction region promoter, or **alphavirus** subgenomic RNA, where the **nucleic acid** molecule is less than 500 **nucleotides** in length;

(8) a host cell comprising the expression cassette of (7);

(9) an RNA vector replicon, comprising:

(a) a 5' sequence which initiates transcription of **alphavirus** RNA;

(b) a **nucleic acid** sequence that codes for biologically active **alphavirus** nonstructural proteins;

(c) an **alphavirus** subgenomic junction region promoter;

(d) a non-**alphavirus** or **alphavirus** **nucleotide** sequence which, when bound by a ligand reduces transcription of subgenomic RNA or translation of a heterologous gene of interest encoded by the subgenomic RNA, where the **alphavirus** **nucleotide** sequence is from a second **alphavirus** different from the first **alphavirus**;

(e) a heterologous gene of interest; and

(f) a 3' **alphavirus** RNA polymerase recognition sequence;

(10) an RNA vector, comprising:

(a) a 5' sequence which initiates transcription of **alphavirus** RNA;

(b) an **alphavirus** subgenomic junction region promoter;

(c) a non-**alphavirus** or **alphavirus** **nucleotide** sequence which, when bound by a ligand reduces transcription of subgenomic RNA or translation of a heterologous gene of interest encoded by the subgenomic RNA;

(d) a heterologous gene of interest; and

(e) a 3' **alphavirus** RNA polymerase recognition sequence, where the RNA vector does not encode all biologically active **alphavirus** nonstructural proteins;

(11) an **alphavirus** vector construct, comprising a 5' promoter operably linked to a **nucleic acid** molecule, where the **nucleic acid** molecule is complementary **DNA** to the RNA vector of (9) or (10);

(12) an expression cassette, comprising a promoter which is operably linked to and transcribes a **nucleic acid** molecule, where the **nucleic acid** molecule comprises the complement of a sequence from a subgenomic 5' end non-translated region of an **alphavirus** RNA vector replicon, and where the transcribed sequence is less than 500 **nucleotides**;

(13) an expression cassette, comprising a promoter which is operably linked to and transcribes a **nucleic acid** molecule, where the **nucleic acid** molecule comprises the complement of a sequence from an **alphavirus** RNA vector replicon, or subgenomic junction region promoter, and where the transcribed sequence is less than 500 **nucleotides**; and

(14) a method for reducing transcription of subgenomic RNA or

translation of a heterologous gene of interest encoded by subgenomic RNA of an **alphavirus** RNA vector replicon or **alphavirus** vector construct, comprising:

(a) introducing an RNA vector of (9) or (10); or an alphavirus vector construct of (11) into a cell; and

(b) introducing into a cell:

(i) a ligand that reduces transcription of subgenomic RNA or translation of a heterologous gene of interest encoded by the subgenomic RNA; or

(ii) an expression cassette which directs the expression of a ligand that reduces transcription of subgenomic RNA or translation of a heterologous gene of interest encoded by the subgenomic RNA, such that transcription of subgenomic RNA or translation of a heterologous gene of interest encoded by subgenomic RNA is reduced.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

No biological data given.

USE - N1 is useful in the development of packaging systems for the high level production of recombinant alphavirus vector particles useful for directing the expression of one or more heterologous gene products. The vectors encoding N1 and the expression cassettes are useful for generating recombinant alphavirus particles and alphavirus packaging cell lines. The RNA vectors and alphavirus constructs are useful for reducing transcription of subgenomic RNA or translation of a heterologous gene of interest encoded by subgenomic RNA of an alphavirus RNA vector replicon, or alphavirus vector construct.

Dwg.0/8

TECH UPTX: 20000818

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Nucleic Acid**: The **signal peptide** is an **alphavirus** E3 peptide or an **alphavirus** 6k **peptide**. Alternatively, the **signal peptide** is a non-**alphavirus signal peptide**, e.g. a tissue plasminogen activator **signal peptide**. The **signal peptide** is a first **signal peptide**. and the **nucleic acid** molecule further comprises a second **signal peptide**. The first **signal peptide** is an **alphavirus** E3 **peptide** and the second **signal peptide** is an **alphavirus** 6k peptide.

Preferred Expression Cassette: In the expression cassette of (12), the **nucleic acid** molecule further comprises at least a portion of the complement of a gene of interest. In the expression cassette of (13), the **nucleic acid** molecule further comprises at least a portion of the gene of interest of the RNA vector replicon, or at least a portion of the nonstructural protein 4 gene of the RNA vector replicon.

Preferred Vector: In the expression vector of (1) and (2), the promoter is a pol II promoter.

The expression vector of (3) further comprises a 5' promoter upstream of the expression cassette which directs the transcription of the expression cassette in a eukaryotic cell.

Optionally, in the vector of (10), the 5' sequence which initiates transcription and the 3' **alphavirus** RNA polymerase recognition sequence are from a first **alphavirus**, and the **alphavirus** **nucleotide** sequence is from a second **alphavirus** different from the first **alphavirus**.

In the vectors of (9) and (10), the non-**alphavirus** **nucleotide** sequence is a binding site for a R17 coat binding protein (e.g. a **nucleotide** sequence of 5TOP or TOP as defined in

the specification), a binding site for an antibiotic such as Tobramycin, or a binding site for Hoechst dyes H33258 or H33342. The **alphavirus nucleotide** sequence is a sequence from a subgenomic 5' end non-translated region of Venezuelan equine encephalitis (VEE). The non-**alphavirus nucleotide** sequence or second **alphavirus nucleotide** sequence is positioned downstream from the **alphavirus** subgenomic junction region promoter or upstream from the heterologous gene of interest. The first **alphavirus** is **Sindbis** virus or a Semliki Forest virus and the second **alphavirus** is VEE (preferred). The RNA vectors further comprise a polyadenylation tract.
Preferred Construct: In the construct of (11), the promoter is a eukaryotic promoter or a bacteriophage promoter.
Preferred Packaging Cell: The **signal peptide** in the first and second expression cassette is a first **signal peptide** and the expression cassettes further comprise a second **signal peptide**. The first **signal peptide** is an **alphavirus** E3 **peptide** and the second **signal peptide** is an **alphavirus** 6k peptide. The packaging cell further comprises EC1.
Preferred Method: The method of (6), further comprises introducing into the cell an expression cassette which, when transcribed produces an RNA sequence complementary to an **alphavirus** junction region promoter, or, **alphavirus** subgenomic RNA.
In the method of (14), the ligand is R17 coat binding protein, an antibiotic such as Tobramycin, a Hoechst dye H33258 or H33342, or an antisense sequence.

L34 ANSWER 21 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-452400 [39] WPIDS
CR 2000-452401 [39]; 2000-465745 [40]
DNC C2000-137949
TI Expression cassettes encoding the human immunodeficiency virus (HIV) Gag-containing polypeptide useful for vaccinating against HIV infections and acquired immunodeficiency syndrome (AIDS).
DC B04 C06 D16
IN BARNETT, S; GREER, C; HARTOG, K; LIAN, Y; LIU, H; SELBY, M; SRIVASTAVA, I; WALKER, C; ZUR MEGEDE, J; ZUR, M J
PA (CHIR) CHIRON CORP
CYC 90
PI WO 2000039302 A2 20000706 (200039)* EN 390p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000022216 A 20000731 (200050)
EP 1141313 A2 20011010 (200167) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ZA 2001005590 A 20020731 (200271) 135p
JP 2002533124 W 20021008 (200281) 386p
ZA 2001005589 A 20021030 (200282) 411p
ADT WO 2000039302 A2 WO 1999-US31245 19991230; AU 2000022216 A AU 2000-22216 19991230; EP 1141313 A2 EP 1999-966727 19991230, WO 1999-US31245 19991230; ZA 2001005590 A ZA 2001-5590 20010706; JP 2002533124 W WO 1999-US31245 19991230, JP 2000-591193 19991230; ZA 2001005589 A ZA 2001-5589 20010706
FDT AU 2000022216 A Based on WO 200039302; EP 1141313 A2 Based on WO 200039302; JP 2002533124 W Based on WO 200039302

PRAI US 1999-168471P 19991201; US 1998-114495P 19981231
AB WO 200039302 A UPAB: 20021220
NOVELTY - Synthetic expression cassettes comprising **nucleic acids** encoding the human immunodeficiency virus (HIV) Gag-containing polypeptide, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) an expression cassette (I) comprising a **polynucleotide** sequence encoding a protein comprising a human immunodeficiency virus (HIV) Gag polypeptide (the **polynucleotide** sequence encoding the Gag polypeptide comprises a sequence with at least 90% sequence identity to a defined 60 **nucleotide** sequence (N1) given in the specification);
(2) a recombinant expression system (II) for use in a host cell comprising (I) operably linked to control elements suitable or protein expression in the host;
(3) a cell (III) comprising (II);
(4) a method (IV) for producing polypeptides including HIV Gag polypeptide sequences, comprising incubating (III) under conditions suitable for expression of the polypeptide;
(5) a method (V) for producing virus-like particles (VLPs), comprising incubating (III) under conditions suitable for production of VLPs; and
(6) a method (VI) for **DNA** vaccination of a subject, comprising introducing (II) into a subject under conditions suitable for gene expression.
ACTIVITY - Anti-HIV.
MECHANISM OF ACTION - Vaccine.
USE - The expression cassettes may be used for the recombinant expression of HIV Gag-polypeptides which may then be used to vaccinate against HIV infection and acquired immunodeficiency syndrome (AIDS).
Dwg.0/82
TECH UPTX: 20000818
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Expression Cassettes: In (I), the **polynucleotide** sequence encoding the Gag polypeptide may alternatively comprise a sequence with at least 90% sequence identity to a defined 1268 or 1515 **nucleotide** sequence ((N2) and (N3) (respectively)) given in the specification. (I) may further comprise:
(i) a **nucleotide** sequence encoding a HIV **protease** polypeptide with at least 90% sequence identity to a defined 1853, 1865 or 1865 **nucleotide** sequence ((N4), (N5) and (N6) (respectively)) given in the specification;
(ii) a **nucleotide** sequence encoding a HIV reverse transcriptase polypeptide with at least 90% sequence identity to a defined 2305, 2299, 2306, 2300 or 2312 **nucleotide** sequence ((N7), (N8), (N9), (N10) and (N11) (respectively)) given in the specification;
(iii) a **nucleotide** sequence encoding a HIV tat polypeptide with at least 90% sequence identity to a defined 101, 306, 306 or 168 **nucleotide** sequence ((N12), (N13), (N14) and (N15) (respectively)) given in the specification; and/or
(iv) a **nucleotide** sequence encoding a HIV polymerase polypeptide with at least 90% sequence identity to a defined 4319 **nucleotide** sequence (N16) given in the specification.
The **nucleotide** sequence encoding the HIV polymerase polypeptide has at least 90% identity to (N3) and the sequence is modified by deletions of coding regions corresponding to reverse transcriptase and integrase. The **polynucleotide** sequence preserves T-helper cell and cytotoxic T-lymphocyte (CTL) groups.
(I) further comprises a sequence encoding a HCV (undefined) core polypeptide which has at least 90% identity to a defined 2031

nucleotide sequence (N17) given in the specification or a sequence encoding a HIV Env (envelope) polypeptide which has at least 90% identity to one of two defined 144 **nucleotide** sequences ((N18) and (N19)) given in the specification. Preferably, the Env polypeptide includes sequences flanking a V1 region but has a deletion in the V1 region itself (in which case it comprises a defined 2538 **nucleotide** sequence (N20) given in the specification) or a sequence flanking a V2 region but has a deletion in the V2 region itself (in which case it comprises one of two defined 2031 and 2553 **nucleotide** sequences ((N20) and (N21)) given in the specification or alternatively one of 7 defined sequences ((N22) to (N28)) given in the specification). Preferably the Env polypeptide comprises sequences flanking a V1/V2 region but has a deletion in the V1/V2 region itself (in which case it comprises one of 10 defined sequences ((N29) to (N38)) given in the specification). The Env polypeptide has a mutated cleavage site that prevents the cleavage of a gp140 polypeptide into a gp120 polypeptide and/or a gp41 polypeptide. Preferably, the polypeptide is either (N30) or one of two defined 2112 and 1863 (respectively) **nucleotide** sequences ((N39) and (N40)) given in the specification or (N24), (N25), (N26), (N35), (N36) and/or (N37) or one of two defined 2025 **nucleotide** sequences ((N41) and (N42)) given in the specification. Preferably, it is a gp160 Env polypeptide of fragment. The **polynucleotide** sequence may be (N20), (N22), (N27), (N28), (N31), (N32), (N38) or one of 5 defined sequences ((N43)-(N46)) given in the specification. The **polynucleotide** sequence may be (N21), (N30), (N40) or one of 5 defined sequences ((N47)-(N51)) given in the specification. The **polynucleotide** sequence may be (N23), (N24), (N25), (N26), (N34), (N35), (N36), (N37), (N41), (N42) or one of 2 defined sequences ((N52) and (N53)) given in the specification.

Preferred Expression Systems: In (II), the control elements are a transcriptional promoter, enhancer or termination signal, a polyadenylation signal, a sequence for optimization of translation initiation and/or a translational termination sequence. The promoter is a cytomegalovirus (CMV), CMV and intron A, SV40, RSV, HIV-Ltr, MMLV-Ltr and/or metallothionein. (II) may be used as a gene delivery vector in mammalian hosts. (II) is preferably an **alpha virus** construct, cDNA vector construct or eukaryotic layered vector initiation system comprising (I).

Preferred Cells: (III) is a mammalian cell (especially a BHK, VERO, HT1080 293, RD, COS-7 and/or CHO cell), insect cell (either Trichoplusia ni (Tn5) or Sf9 cell), bacterial cell, yeast cell, plant cell or an antigen presenting cell. Preferably, it is a lymphoid cell (macrophage, monocyte, dendritic cell, B-cell, T-cell, stem cell (or progenitors of them)), primary cell, immortalized cell or a tumor derived cell. (III) is used for packaging lentivirus vectors.

Preferred Methods: (V) may further comprise purifying the VLPs.

In (VI), (II) is a non-viral vector delivered using a particulate carrier, i.e. the vector is coated onto a gold or tungsten particle and delivered using a gene gun. The vector may be encapsulated in a liposome preparation. IT may also be a non-viral vector (especially retroviral or lentiviral). The subject is a mammal (especially human). The polypeptide is expressed from the vector and initiates an immune response. **Transfection** may be carried out ex vivo (and the cells reintroduced into the subject) or in vivo. The response is a humoral response or a cellular immune response.

Preparation: The vectors and the proteins they encode may be produced according to standard recombinant **DNA** methodologies.

L34 ANSWER 22 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-414600 [36] WPIDS

DNC C2000-125801
TI Attenuated bovine viral diarrhea virus, used as a vaccine to give cattle protective immunity against subsequent infection with the virus.
DC B04 C06 D16
IN CAO, X; SHEPPARD, M G
PA (PFIZ) PFIZER PROD INC; (PFIZ) PFIZER INC
CYC 34
PI EP 1013757 A2 20000628 (200036)* EN 44p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 9958376 A 20000511 (200036)
JP 2000139482 A 20000523 (200036) 43p
CA 2287775 A1 20000510 (200040) EN
CN 1254756 A 20000531 (200045)
US 6168942 B1 20010102 (200103)
BR 9905352 A 20010206 (200111)
MX 9910304 A1 20000501 (200129)
NZ 500925 A 20010629 (200140)
ZA 9907011 A 20010627 (200140) 54p
US 6410032 B1 20020625 (200246)
US 6410299 B1 20020625 (200246)
ADT EP 1013757 A2 EP 1999-308866 19991108; AU 9958376 A AU 1999-58376 19991109; JP 2000139482 A JP 1999-319340 19991110; CA 2287775 A1 CA 1999-2287775 19991108; CN 1254756 A CN 1999-123522 19991110; US 6168942 B1 Provisional US 1998-107908P 19981110, US 1999-433262 19991104; BR 9905352 A BR 1999-5352 19991110; MX 9910304 A1 MX 1999-10304 19991109; NZ 500925 A NZ 1999-500925 19991109; ZA 9907011 A ZA 1999-7011 19991109; US 6410032 B1 Provisional US 1998-107908P 19981110, Div ex US 1999-433262 19991104, US 2000-702330 20001031; US 6410299 B1 Provisional US 1998-107908P 19981110, Div ex US 1999-433262 19991104, US 2000-649796 20000829
FDT US 6410032 B1 Div ex US 6168942; US 6410299 B1 Div ex US 6168942
PRAI US 1998-107908P 19981110; US 1999-433262 19991104; US 2000-702330 20001031; US 2000-649796 20000829
AB EP 1013757 A UPAB: 20000801
NOVELTY - An attenuated bovine diarrhea (BVD) virus (I), having a genomic **nucleic acid** sequence comprising **nucleotides** 39-12116 of a 14078 **nucleotide** wildtype BVD virus sequence, fully defined in the specification, or a degenerate variant of it, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a host cell infected with (I);
(2) a **nucleic acid** molecule (II), comprising **nucleotides** 39-12116 of the fully defined 14078 **nucleotide** sequence;
(3) a vector (III) comprising (II);
(4) a host cell transformed, or **transfected**, with (II) or (III);
(5) modifying an isolated wildtype BVD genome, or attenuating a wildtype BVD virus, for use in a vaccine, comprising mutating the genomic **nucleic acid** to inactivate the Npro **protease** gene;
(6) a BVD **viral genome** (IV) and attenuated BVD virus (V), produced by the method of (5);
(7) a vector (VI) comprising (IV);
(8) a host cell comprising (IV), (V) or (VI);
(9) progeny virus produced by the host cell of (1), (4) or (8);
(10) a vaccine comprising (I), (II), (IV), or (V), and a carrier;
(11) inducing production of an antibody to BVD virus, comprising administering (I), (II), (III), (IV), (V), or (VI), to an animal; and
(12) an antibody produced by the method of (11).

ACTIVITY - Antiviral.

MECHANISM OF ACTION - Vaccine producing a protective immunity due to a humoral and cell-mediated immune response. BVDdN1 virus was administered to cattle subcutaneously as a dosage of 107TCID50/animal in 2.0 ml MDBK cell lysate. A second vaccine dose was administered after 28 days. Blood samples were collected from the animals at regular intervals, and serum neutralizing antibodies were detected by Sn assay. After the two dose vaccination, all of the animals reached a positive titer of 1:64 or higher after 7 days, and subsequently maintained a similar seroconversion level over the 13 weeks of testing. These results show that BVDdN1 virus is able to replicate in cattle, and induce a positive neutralization serum for the virus.

USE - Vaccines comprising (I), (II), (IV), or (V), are used to provide cattle with protective immunity against subsequent infection with the BVD virus (claimed).

ADVANTAGE - Prior art vaccines using chemically inactivated viruses require multiple doses to achieve primary infection for a short period of time, the attenuated virus requires fewer administrations.

Dwg.0/3

TECH UPTX: 20000801

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Virus: (I) is substantially purified.

Preferred method: The inactivation of Npro **protease** gene, comprises reverse transcribing the genomic RNA from the wildtype virus to produce cDNA, cloning the cDNA, mutating the Npro **protease** gene in the cloned cDNA so that no active gene product is produced, and cloning the mutated cDNA. The gene is inactivated by deleting all or part of its sequence from the genome.

Preferred Antibody: The antibody is produced in cattle, and is isolated from the animal after production/

L34 ANSWER 23 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-350743 [30] WPIDS
DNN N2000-262746 DNC C2000-106769
TI Isolated **polynucleotide** encoding a Chlamydia polypeptide useful to treat, diagnose and prevent disease caused by Chlamydia infection.
DC B04 D16 S03
IN DUNN, P L; MURDIN, A D; OOMEN, R P
PA (CONN-N) CONNAUGHT LAB LTD; (AVET) AVENTIS PASTEUR LTD; (DUNN-I) DUNN P L; (MURD-I) MURDIN A D; (OOME-I) OOMEN R P
CYC 91
PI WO 2000024902 A1 20000504 (200030)* EN 101p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 9963598 A 20000515 (200039)
EP 1124965 A1 20010822 (200149) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002102270 A1 20020801 (200253)
JP 2002528082 W 20020903 (200273) 114p
ADT WO 2000024902 A1 WO 1999-GB3571 19991028; AU 9963598 A AU 1999-63598 19991028; EP 1124965 A1 EP 1999-951023 19991028, WO 1999-GB3571 19991028; US 2002102270 A1 Provisional US 1998-106046P 19981028, Provisional US 1999-132271P 19990503, Div ex US 1999-427533 19991026, US 2001-779081 20010208; JP 2002528082 W WO 1999-GB3571 19991028, JP 2000-578454 19991028
FDT AU 9963598 A Based on WO 200024902; EP 1124965 A1 Based on WO 200024902;

JP 2002528082 W Based on WO 200024902
PRAI US 1999-427533 19991026; US 1998-106046P 19981028; US 1999-132271P 19990503; US 2001-779081 20010208
AB WO 200024902 A UPAB: 20000624
NOVELTY - An isolated **polynucleotide** (N1) encoding a 98 kDa outer membrane protein of a strain of Chlamydia pneumoniae, is new.
DETAILED DESCRIPTION - An isolated **polynucleotide** (N1) has a **nucleotide** sequence which comprises:
(a) a defined **nucleotide** sequence (I) of 3050 base pairs or functional fragments of (I);
(b) a **polynucleotide** sequence encoding a polypeptide with a sequence at least 75% homologous to (II) which has a defined protein sequence of 931 amino acids, or functional fragments; or
(c) a sequence capable of hybridizing under stringent conditions to a sequence comprising (I), or functional fragments.
INDEPENDENT CLAIMS are also included for the following:
(1) an isolated polypeptide (P1) with a sequence at least 75% homologous to (II), or functional fragments of (II);
(2) a polypeptide P2 comprising P1 linked to a fusion polypeptide;
(3) an expression cassette comprising N1 operably linked to a promoter;
(4) an expression vector comprising the expression cassette of (3);
(5) a host cell comprising the expression cassette of (3);
(6) a method of producing a recombinant polypeptide with sequence (II) comprising culturing the host cell of (5) and recovering the polypeptide;
(7) a vaccine vector comprising the expression cassette of (3);
(8) a pharmaceutical composition containing P1 and one or more known Chlamydia antigens;
(9) a method for inducing an immune response in a mammal comprising administering the vaccine vector of (7) or a composition containing P1 to induce an immune response;
(10) a **polynucleotide** probe reagent capable of detecting the presence of Chlamydia in biological material comprising a **polynucleotide** that hybridizes to N1 under stringent conditions;
(11) a hybridization method for detecting the presence of Chlamydia in a sample comprising:
(a) obtaining **polynucleotide** from the sample;
(b) hybridizing the obtained **polynucleotide** with the **polynucleotide** probe reagent of (10) under conditions allowing hybridization of the probe and the sample; and
(c) detecting any hybridization occurring;
(12) an amplification method for detecting the presence of Chlamydia in a sample comprising:
(a) obtaining **polynucleotide** from the sample;
(b) amplifying the **polynucleotide** using one or more **polynucleotide** probe reagents of (10); and
(c) detecting the amplified **polynucleotide**;
(13) a method for detecting the presence of Chlamydia in a sample comprising contacting the sample with a detecting reagent that binds to P1 in the sample and detecting the formed complex;
(14) an affinity chromatography method for substantially purifying a polypeptide with sequence (II) comprises:
(a) contacting a sample containing (II) with a detecting reagent that binds to the polypeptide to form a complex;
(b) isolating the formed complex;
(c) dissociating the formed complex; and
(d) isolating the dissociated polypeptide; and
(15) an antibody that immunospecifically binds P1 or a fragment or derivative of the antibody containing its binding domain.

ACTIVITY - Antibacterial.
MECHANISM OF ACTION - Vaccine.
Balb/c mice (7-9 weeks old) were immunized intramuscularly and intranasally with plasmid DNA containing the coding sequence of C. pneumoniae 98 kDa outer membrane protein gene. Control animals were given saline or the plasmid vector without the chlamydial gene. The intramuscular immunization comprised 100 micro g DNA in 50 micro l phosphate buffered saline (PBS) at 0, 3 and 6 weeks and the intranasal immunization comprised 50 micro g DNA in 50 micro l PBS at 0, 3 and 6 weeks. At week 8, immunized mice were inoculated intranasally with 5x105 inclusion forming units (IFU) of C. pneumoniae, strain AR39 in 100 micro l SPG (sucrose, glutamate, phosphate) buffer. Lungs were taken from the mice at day 9 post challenge and homogenized in SPG buffer, the homogenate was assayed for the presence of infectious chlamydia by inoculation onto monolayers of susceptible cells After incubation the monolayers were fixed and immunoperoxidase stained for the presence of chlamydial inclusions using convalescent sera from rabbits infected with C. pneumoniae and metal-enhanced DAB (not defined) as a peroxidase substrate. Mice immunized with the plasmid containing the 98 kDa outer membrane protein gene had chlamydial lung titers less than 300000 IFU/lung at day 5 and less than 144000 at day 9 compared to 685240 IFU/lung at day 5 and 238080 at day 9 for the control mice immunized with saline.
USE - The polynucleotides and polypeptides can be used as a vaccine for humans to treat or prevent disease caused by Chlamydia infection and P1, N1 or an antibody to P1 can be used to diagnose a Chlamydia infection.
Dwg.0/4

TECH UPTX: 20000624
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Nucleotide**: N1 is linked to a second **nucleotide** sequence encoding a fusion polypeptide which is a heterologous **signal peptide**, used to facilitate purification.
N1 encodes a functional fragment of the 98 kDa outer membrane polypeptide with sequence (II).
Preferred Polypeptide: P1 preferably has sequence (II) or functional fragments of (II).
The fusion polypeptide P2 comprises a heterologous polypeptide with adjuvant activity or a **signal peptide**, used to facilitate purification..
Preferred Cell: The host cell is a prokaryotic or eukaryotic cell.
Preferred Probe: The **polynucleotide** probe reagent is a **DNA** primer. The probe may be immobilized on a solid support and may be labelled by radioactive isotopes, enzymes, or fluorogenic or luminescent compounds. The probe is generally 10-40 **nucleotides** long.
Preferred Method: Detecting the presence of Chlamydia in a sample through complex formation with P1 and the affinity chromatography method both use a monoclonal or polyclonal antibody as the detecting reagent. The sample detected may be a blood sample.
Preferred Vector: The vaccine vector is a live bacterial or viral vaccine vector e.g. pox virus, **alphavirus**, Salmonella typhimurium or Vibrio cholerae vector.

L34 ANSWER 24 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-350742 [30] WPIDS
DNN N2000-262745 DNC C2000-106768
TI Isolated **polynucleotide** encoding a Chlamydia polypeptide useful to treat, diagnose and prevent disease caused by Chlamydia infection.
DC B04 D16 S03
IN DUNN, P L; MURDIN, A D; OOMEN, R P
PA (CONN-N) CONNAUGHT LAB LTD; (AVET) AVENTIS PASTEUR LTD; (DUNN-I) DUNN P L;

(MURD-I) MURDIN A D; (OOME-I) OOMEN R P
CYC 91
PI WO 2000024901 A1 20000504 (200030)* EN 88p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 9963593 A 20000515 (200039)
EP 1124964 A1 20010822 (200149) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6403101 B1 20020611 (200244)
US 2002091096 A1 20020711 (200248)
JP 2002528081 W 20020903 (200273) 104p
ADT WO 2000024901 A1 WO 1999-GB3565 19991028; AU 9963593 A AU 1999-63593 19991028; EP 1124964 A1 EP 1999-951017 19991028, WO 1999-GB3565 19991028; US 6403101 B1 Provisional US 1998-106037P 19981028, Provisional US 1999-154658P 19990920, US 1999-427501 19991026; US 2002091096 A1 Provisional US 1998-106037P 19981028, Provisional US 1999-154658P 19990920, Div ex US 1999-427501 19991026, US 2001-905119 20010713; JP 2002528081 W WO 1999-GB3565 19991028, JP 2000-578453 19991028
FDT AU 9963593 A Based on WO 200024901; EP 1124964 A1 Based on WO 200024901; JP 2002528081 W Based on WO 200024901
PRAI US 1999-427501 19991026; US 1998-106037P 19981028; US 1999-154658P 19990920; US 2001-905119 20010713
AB WO 200024901 A UPAB: 20000624
NOVELTY - An isolated **polynucleotide** (N1) encoding a lorf2 protein of a strain of Chlamydia pneumoniae, is new.

DETAILED DESCRIPTION - An isolated **polynucleotide** (N1) has a **nucleotide** sequence which comprises:

(a) a defined **nucleotide** sequence (I) of 1550 base pairs or functional fragments of (I);

(b) a **nucleotide** sequence encoding a polypeptide with a sequence at least 75% homologous to (II) which has a defined protein sequence of 422 amino acids, or functional fragments; or

(c) a sequence capable of hybridizing under stringent conditions to a sequence comprising (I), or functional fragments.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide (P1) with a sequence at least 75% homologous to (II), or functional fragments of (II);

(2) a polypeptide P2 comprising P1 linked to a fusion polypeptide;

(3) an expression cassette comprising N1 operably linked to a promoter;

(4) an expression vector comprising the expression cassette of (3);

(5) a host cell comprising the expression cassette of (3);

(6) a method of producing a recombinant polypeptide with sequence (II) comprising culturing the host cell of (5) and recovering the polypeptide;

(7) a vaccine vector comprising the expression cassette of (3);

(8) a pharmaceutical composition containing P1 and one or more known Chlamydia antigens;

(9) a method for inducing an immune response in a mammal comprising administering the vaccine vector of (7) or a composition containing P1 to induce an immune response;

(10) a **polynucleotide** probe reagent capable of detecting the presence of Chlamydia in biological material comprising a **polynucleotide** that hybridizes to N1 under stringent conditions;

(11) a hybridization method for detecting the presence of Chlamydia

in a sample comprising:
(a) obtaining **polynucleotide** from the sample;
(b) hybridizing the obtained **polynucleotide** with the **polynucleotide** probe reagent of (10) under conditions allowing hybridization of the probe and the sample; and
(c) detecting any hybridization occurring;
(12) an amplification method for detecting the presence of Chlamydia in a sample comprising:
(a) obtaining **polynucleotide** from the sample;
(b) amplifying the **polynucleotide** using one or more **polynucleotide** probe reagents of (10); and
(c) detecting the amplified **polynucleotide**;
(13) a method for detecting the presence of Chlamydia in a sample comprising contacting the sample with a detecting reagent that binds to P1 in the sample and detecting the formed complex;
(14) an affinity chromatography method for substantially purifying a polypeptide with sequence (II) comprises:
(a) contacting a sample containing (II) with a detecting reagent that binds to the polypeptide to form a complex;
(b) isolating the formed complex;
(c) dissociating the formed complex; and
(d) isolating the dissociated polypeptide; and
(15) an antibody that immunospecifically binds P1 or a fragment or derivative of the antibody containing its binding domain.
ACTIVITY - Antibacterial.
MECHANISM OF ACTION - Vaccine.
Balb/c mice (7-9 weeks old) were immunized intramuscularly and intranasally with plasmid DNA containing the coding sequence of C. pneumoniae lorf2 gene. Control animals were given saline or the plasmid vector without the chlamydial gene. The intramuscular immunization comprised 100 micro g DNA in 50 micro l phosphate buffered saline (PBS) at 0, 3 and 6 weeks and the intranasal immunization comprised 50 micro g DNA in 50 micro l PBS at 0, 3 and 6 weeks. At week 8, immunized mice were inoculated intranasally with 5x105 inclusion forming units (IFU) of C. pneumoniae, strain AR39 in 100 micro l SPG (sucrose, glutamate, phosphate) buffer. Lungs were taken from the mice at day 9 post challenge and homogenized in SPG buffer, the homogenate was assayed for the presence of infectious chlamydia by inoculation onto monolayers of susceptible cells After incubation the monolayers were fixed and immunoperoxidase stained for the presence of chlamydial inclusions using convalescent sera from rabbits infected with C. pneumoniae and metal-enhanced DAB (not defined) as a peroxidase substrate. Mice immunized with the plasmid containing the lorf2 gene had an average chlamydial lung titer of 11050 IFU/lung compared to 111783 IFU/lung for the control mice immunized with saline.
USE - The polynucleotides and polypeptides can be used as a vaccine for humans to treat or prevent disease caused by Chlamydia infection and P1, N1 or an antibody to P1 can be used to diagnose a Chlamydia infection.
Dwg.0/4

TECH UPTX: 20000624
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Nucleotide**: N1 is linked to a second **nucleotide** sequence encoding a fusion polypeptide which is a heterologous **signal peptide**, used to facilitate purification.
N1 encodes a functional fragment of the lorf2 polypeptide with sequence (II).
Preferred Polypeptide: P1 preferably has sequence (II) or functional fragments of (II).
The fusion polypeptide P2 comprises a heterologous polypeptide with adjuvant activity or a **signal peptide**, used to facilitate purification..

Preferred Cell: The host cell is a prokaryotic or eukaryotic cell.
Preferred Probe: The **polynucleotide** probe reagent is a **DNA** primer. The probe may be immobilized on a solid support and may be labelled by radioactive isotopes, enzymes, or fluorogenic or luminescent compounds. The probe is generally 10-40 **nucleotides** long.
Preferred Method: Detecting the presence of Chlamydia in a sample through complex formation with P1 and the affinity chromatography method both use a monoclonal or polyclonal antibody as the detecting reagent. The sample detected may be a blood sample.
Preferred Vector: The vaccine vector is a live bacterial or viral vaccine vector e.g. pox virus, **alphavirus**, Salmonella typhimurium or Vibrio cholerae vector.

L34 ANSWER 25 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-224703 [19] WPIDS
DNN N2000-168305 DNC C2000-068764
TI Novel antigens and corresponding **DNA** molecules that can be used to prevent, treat and diagnose disease caused by Chlamydia infection in mammals, especially humans.
DC B04 D16 S03
IN MURDIN, A D; OOMEN, R P
PA (CONN-N) CONNAUGHT LAB LTD; (AVET) AVENTIS PASTEUR LTD
CYC 89
PI WO 2000011183 A2 20000302 (200019)* EN 201p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9952973 A 20000314 (200031)
EP 1104470 A2 20010606 (200133) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002523049 W 20020730 (200264) 225p
ADT WO 2000011183 A2 WO 1999-IB1449 19990818; AU 9952973 A AU 1999-52973 19990818; EP 1104470 A2 EP 1999-938465 19990818, WO 1999-IB1449 19990818; JP 2002523049 W WO 1999-IB1449 19990818, JP 2000-566437 19990818
FDT AU 9952973 A Based on WO 200011183; EP 1104470 A2 Based on WO 200011183; JP 2002523049 W Based on WO 200011183
PRAI US 1999-376770 19990817; US 1998-97187P 19980820; US 1998-97188P 19980820; US 1998-97189P 19980820; US 1998-97190P 19980820; US 1998-97195P 19980820; US 1998-97196P 19980820; US 1998-97197P 19980820; US 1998-97191P 19980827
AB WO 200011183 A UPAB: 20021105
NOVELTY - Isolated Chlamydia pneumoniae polypeptides (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII) are new. All sequences are fully disclosed in the specification.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a **polynucleotide** (PN) encoding a (PP) having a sequence that is at least 75% homologous to and/or a functional fragment of the (aa) selected from (I)-(VIII), where the (PN) comprises one of the **nucleotide** sequences of 650-3200 base pairs (bp) (IX)-(XVI);
(2) (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII) linked to a fusion polypeptide;
(3) an expression cassette comprising one of the **nucleotide** sequences of 650-3200 base pairs (bp) (IX)-(XVI) operably linked to a promoter;

(4) an expression vector comprising (3);
(5) a host cell comprising (3);
(6) producing a recombinant (PP), comprising:
(a) culturing (5), to allow expression of the (PP); and
(b) recovering the recombinant (PP);
(7) a vaccine vector comprising the (3);
(8) a (PN) probe reagent capable of detecting the presence of Chlamydia in biological material, comprising a (PN) that hybridizes to the (PN) that comprises one of the **nucleotide** sequences of 650-3200 base pairs (bp) (IX)-(XVI);
(9) a hybridization method for detecting the presence of Chlamydia in a sample, comprising:
(a) obtaining (PN) from the sample;
(b) hybridizing the (PN) of with (8); and
(c) detecting the hybridization of (8) with a (PN) in the sample;
(10) an amplification method for detecting the presence of Chalmydia in sample, comprising:
(a) see (9) (a);
(b) amplifying the (PN) using one or more (8); and
(c) detecting the amplified (PP) (sic);
(11) detecting the presence of Chlamydia in a sample comprising:
(a) contacting the sample with a detecting reagent that binds to a (PP) to form a complex (C), the (PP) being selected from the following: (CPN 100)111, 224, 230, 231, 232, 235, 394, and 395; and
(b) detecting (C);
(12) an affinity chromatography method for substantially purifying a Chlamydia antigen comprising:
(a) contacting a sample containing the Chalmydia antigen with a detecting reagent that binds to a (PP) to form a (C), the (PP) being selected from the (PP) in (11) (a);
(b) isolating (C);
(c) dissociating (C); and
(d) isolating the dissociated Chlamydia antigen; and
(13) an antibody (ab) immunospecific for (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII), or a fragment or derivative of the (ab) containing the binding domain of the (ab).

ACTIVITY - Antibacterial; anti-pneumonia; antitussive; antiasthmatic. No biological data given.

MECHANISM OF ACTION - Vaccine. No biological data given.

USE - Isolated Chlamydia polypeptides (PP) may be used to prevent, treat and detect the presence of Chlamydia infection and/or the presence of Chlamydia in a sample. The (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII) may be used to induce an immune response in a mammal. The vaccine vector comprising a polynucleotide (PN) where the (PN) comprises one of the nucleotide sequences of 650-3200 base pairs (bp) (IX)-(XVI) given in the specification is used to induce an immune response in a mammal. The (PN) probe is capable of detecting the presence of Chlamydia in biological material. (All claimed). The antibody may also be used therapeutically to treat and/or prevent a Chlamydia infection. The above compositions may also be used for veterinary treatment, for example, to treat and/or prevent Chlamydia infections in cats and dogs.

ADVANTAGE - There is increasing evidence that Chlamydia pneumoniae may be linked to other diseases/conditions including chronic bronchitis, asthma and sinusitis and can lead to hospitalization in patients with underlying illness, as well as non-respiratory diseases. Several studies have shown a correlation of previous infections with C.pneumoniae and heart attacks, coronary artery and carotid artery disease. (See, Fong et al., (1997) Journal of Clinical Microbiology 35:48). Therefore, the vaccine disclosed may have further indirect clinical applications and

concomitant advantages, for example, reducing the likelihood of heart disease while preventing C.pneumoniae infection (No biological data is given). Antibiotic resistance is increasingly common and the vaccine preparation provides an alternative method of treatment. Further, exposure to other Chlamydia.spp affords no cross-protection to C.pneumoniae infection.
Dwg.0/16

TECH UPTX: 20000419

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: The (PP) are prepared using standard recombinant techniques comprising transfection of a suitable host cell and culturing the host cell under suitable conditions to allow the expression of the (PP). (See, Current Protocols in Molecular Biology, John Wiley and Sons Inc. (1994)).
The antibody may be produced using standard immunological methods and may also be synthesized recombinantly.
Preferred **Nucleic Acids**: The (PN) may be linked to a second **nucleotide** sequence encoding a fusion polypeptide. The (PN) probe reagent is a **DNA** primer. The (live) vaccine vectors , include, pox virus, **alphavirus**, Salmonella typhimurium, or Vibrio cholerae vector, containing a (PN) of the invention.
Preferred Polypeptides: The fusion (PP) is a (heterologous) **signal peptide** (having adjuvant activity). The recombinant (PP) produced by the above method (6) are selected from the group consisting of (CPN 100)111, 224, 230, 231, 232, 235, 394, and 395. (PP) include those permanently found in the (external vicinity of the) bacterial membrane structure, those permanently found in the (external vicinity of the) inclusion membrane structure, and those that are released into the cytoplasm of the infected cell.
Preferred Host Cell: Preferably, a prokaryotic host cell such as ~~Escherichia coli is used.~~
Preferred Antibody: The antibody may be monoclonal and/or polyclonal, and is preferably of the IgG type for use in a purification method and of the IgA isotype for therapeutic applications.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The (PP) may be prepared synthetically using standard (solid-phase) techniques.

L34 ANSWER 26 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-182719 [16] WPIDS
DNC C2000-057316
TI Novel screen comprising a pool of vectors with randomly modified **nucleotide** sequences, useful for identifying modulators of enzyme activity useful for selecting antibiotic agents.
DC B04 D13 D15 D16
IN HALKIER, T; JENSEN, A; JESPERSEN, L
PA (INOX-N) INOXELL AS; (MEBI-N) M & E BIOTECH AS; (PHAR-N) PHARMEXA AS
CYC 87
PI WO 2000005406 A1 20000203 (200016)* EN 136p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9948985 A 20000214 (200029)
EP 1098991 A1 20010516 (200128) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2001000300 A 20010319 (200129)
CZ 2001000210 A3 20010613 (200138)

HU 2001002457 A2 20011029 (200175)
SK 2001000069 A3 20011203 (200203)
ZA 2001000195 A 20020327 (200230) 188p
KR 2001103560 A 20011123 (200232)
JP 2002521652 W 20020716 (200261) 133p
AU 751055 B 20020808 (200263)
EP 1098991 B1 20020911 (200264) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 69902924 E 20021017 (200276)

ADT WO 2000005406 A1 WO 1999-DK408 19990716; AU 9948985 A AU 1999-48985 19990716; EP 1098991 A1 EP 1999-932689 19990716, WO 1999-DK408 19990716; NO 2001000300 A WO 1999-DK408 19990716, NO 2001-300 20010118; CZ 2001000210 A3 WO 1999-DK408 19990716, CZ 2001-210 19990716; HU 2001002457 A2 WO 1999-DK408 19990716, HU 2001-2457 19990716; SK 2001000069 A3 WO 1999-DK408 19990716, SK 2001-69 19990716; ZA 2001000195 A ZA 2001-195 20010108; KR 2001103560 A KR 2001-700871 20010119; JP 2002521652 W WO 1999-DK408 19990716, JP 2000-561352 19990716; AU 751055 B AU 1999-48985 19990716; EP 1098991 B1 EP 1999-932689 19990716, WO 1999-DK408 19990716, Related to EP 2002-76171 19990716; DE 69902924 E DE 1999-602924 19990716, EP 1999-932689 19990716, WO 1999-DK408 19990716

FDT AU 9948985 A Based on WO 200005406; EP 1098991 A1 Based on WO 200005406; CZ 2001000210 A3 Based on WO 200005406; HU 2001002457 A2 Based on WO 200005406; SK 2001000069 A3 Based on WO 200005406; JP 2002521652 W Based on WO 200005406; AU 751055 B Previous Publ. AU 9948985, Based on WO 200005406; EP 1098991 B1 Based on WO 200005406; DE 69902924 E Based on EP 1098991, Based on WO 200005406

PRAI US 1998-94868P 19980729; DK 1998-956 19980720

AB WO 200005406 A UPAB: 20021105

NOVELTY - Cell screen (I) comprising using a pool of expression vectors, each with one member from a library of randomly modified **nucleotide** sequence (NS) encoding a scaffold portion of a parent peptide or RNA.

DETAILED DESCRIPTION - The screen (I) identifies an in vivo modulator of a target enzyme by preparing a pool of expression vectors, transforming a population of substantially identical cells harboring the enzyme, culturing the cells and isolating transformed cells where activity of the enzyme is modulated. The modulator is identified by determining a randomly modified vector NS and/or by determining the amino acid (aa) or RNA sequence of the expression product encoded by NS.

INDEPENDENT CLAIMS are also included for the following:

(1) preparation of replicable vector;
(2) cells transformed by the vector of (1);
(3) producing an enzyme modulator comprising:
(a) growing a cell as in (2); and
(b) harvesting the expression product; or
(c) identifying the modulator according to (I); and
(d) synthesizing the modulator; and
(4) isolating and/or identifying a target biomolecule (M1) using the modulator as an affinity ligand in an affinity purification step, or as a probe against a **cDNA library** derived from the cells harboring the enzyme or as bait in a two- or three-hybrid system.

USE - The screen is used for identification of modulators which in turn are used in selecting a chemical compound, a drug candidate in drug development (claimed). The compound is utilized for preparing a medicinal product (claimed). Modulators are further used for developing a medicinal product by serving as an interaction probe for identification of putative drug candidates in drug discovery phase (claimed) and thus antibiotic and antifungal agents are identified. Modulators are also used for identifying biomolecules which can be used for improving an industrial fermentation

process.

DESCRIPTION OF DRAWING(S) - The diagram shows a schematic representation of pCMVbipep/CI-2A with the functional cis-elements found in pCMVbipep indicated.

Dwg.1/7

TECH UPTX: 20000330

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Nucleotide** Sequence: The randomly modified NSs comprise the invariable part of a parent **nucleotide** encoding truncations in a peptide, optionally with disulfide bridges, random **nucleotides** comprise insertions, preferably single **nucleotide** insertions at specific sites of the parent NS, or substitutions in the parent NS, optionally with a deletion and they range from 3-100 **nucleotides**.

Preferred Random **Nucleotides**: The random **nucleotides** are synthetic completely random **deoxyribonucleotides**, or synthetic limitedly randomized **DNA** sequences (avoiding undesired stop codons and facilitating post-translational modifications and synthetic sequences are) coupled to a sequence encoding a purification tag, and a CDR encoding NS (preferably the CDR-3 peptide sequence from a library of immune-competent cells raised against an antigen). Random **nucleotides** are introduced into the active site of the parent peptide of RNA or into a part encoding a structure interfering with this site. Random **nucleotides** are introduced into the vectors by site directed PCR-mediated mutagenesis. Random **nucleotides** are coupled with one **fusion** partner, a sorting signal like **signal** patch or **peptide**, or a targeting sequence for facilitating expression, purification, isolation and stabilization like His6, myc, BSP biotinylation target sequence, BirA, flu, lacZ or GST tag. A sorting signal helps in exporting expressed peptide out of cells or cell membrane and in eukaryotic cells into organelles.

Preferred Parent Compound: Parent NS encodes a scaffold portion of the parent peptide of RNA, which stabilizes the fragment.

Preferred Modulator: The modulator is stable towards proteolytic attack and/or is insensitive to a reducing environment. The modulator reduces or increases Vmax and Km of the enzyme for at least 1 substrate and is preferably BPTI/Kunitz family **protease** inhibitor, a serpin, Kazal family, soyabean trypsin inhibitor, potato inhibitor, Bowman-Birk, squash inhibitor, wap-type Four-disulfide Core', hirudin factor Xa inhibitor, Ascaris trypsin inhibitor, crystatin, calapin cysteine, tissue inhibitor of metalloproteinases, carboxypeptidase inhibitor, metallocarboxypeptidase inhibitor, angiotensin-converting enzyme inhibitor, cerealalpha-amylase/trypsin inhibitor, thaumatin homologues, alpha-amylase/subtilisin inhibitor, insect alpha-amylase inhibitor, mammalian alpha-amylase from Streptomyces, trehalase inhibitor, polygalacturonase inhibitor and fucosyltransferase, protein kinase C, cAMP-dependent protein kinase, cyclic **nucleotide** phosphodiesterase, protein phosphatease, TCD/MRS6 GDP dissociation, ATPase, ribonuclease, RNA polymerase, **DNA** entry nuclease, phospholipase A2 or beta-lactamase inhibitor. The screen further comprises resolving the 3-dimensional strutur of the identified modulator.

Preferred Cells: The cell harboring the enzyme is a fungal, protozoan, plant and animal cells preferably mammalian insect (arthropod), avian and piscine cell, preferably transformed with one single copy of the vector of (1)

Preferred Vector: The vector of (1) is transformed into a mammalian cell and is a vaccinia **virus**, adenovirus, adeno associated **virus**, herpes simplex **virus**, **alpha** **virus**, semliki forest **virus** vector and more preferably retroviral vector (RV). RV is **transfected** into packaging cells, the virions produced from them are transduced into cells. Virions can be

pseudotyped retrovirus for conferring broad tropism which is produced by an ecotropic packaging cell line or by an ecotropic receptor introduced into cells.

L34 ANSWER 27 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-038358 [03] WPIDS
CR 1995-382985 [49]; 1998-286866 [25]; 1999-229499 [19]; 1999-229532 [19]; 1999-229533 [19]; 1999-254381 [21]; 1999-254713 [21]; 1999-302739 [25]; 1999-326705 [27]; 1999-337420 [28]; 1999-347718 [29]; 1999-371118 [31]; 1999-404743 [34]; 1999-430385 [36]; 1999-551358 [46]; 1999-580306 [49]; 1999-620728 [53]; 2000-062031 [05]; 2000-072883 [06]; 2000-116314 [10]; 2000-237871 [20]; 2000-271386 [23]; 2000-271431 [23]; 2000-271434 [23]; 2000-271435 [23]; 2000-292842 [25]; 2000-317943 [27]; 2000-412154 [35]; 2000-412324 [35]; 2000-412325 [35]; 2000-431586 [37]; 2000-442668 [38]; 2000-452188 [39]; 2000-452395 [39]; 2000-499263 [44]; 2000-572269 [53]; 2000-572270 [53]; 2000-572271 [53]; 2000-587437 [55]; 2000-594320 [56]; 2000-594321 [56]; 2000-611443 [58]; 2000-611444 [58]; 2000-628263 [60]; 2000-638138 [61]; 2000-638201 [61]; 2000-679484 [66]; 2001-016509 [02]; 2001-025022 [03]; 2001-025251 [03]; 2001-025253 [03]; 2001-032160 [04]; 2001-050025 [06]; 2001-050091 [06]; 2001-070561 [08]; 2001-071075 [08]; 2001-071078 [08]; 2001-071395 [08]; 2001-081051 [09]; 2001-090793 [10]; 2001-091968 [10]; 2001-103149 [11]; 2001-183260 [18]; 2001-226690 [23]; 2001-226823 [23]; 2001-235264 [24]; 2001-381383 [40]; 2001-381384 [40]; 2001-408281 [43]; 2001-451708 [48]; 2001-541567 [60]; 2001-541628 [60]; 2001-602746 [68]; 2001-625876 [72]; 2002-075461 [10]; 2002-090516 [12]; 2002-130120 [17]; 2002-130151 [17]; 2002-130882 [17]; 2002-171999 [22]; 2002-172001 [22]; 2002-205567 [26]; 2002-256031 [30]; 2002-280917 [32]; 2002-280928 [32]; 2002-280940 [32]; 2002-292065 [33]; 2002-362426 [39]; 2002-383270 [41]; 2002-404358 [43]; 2002-487624 [52]; 2002-657277 [70]; 2002-665999 [71]; 2002-673823 [72]; 2002-690475 [74]; 2002-713224 [77]; 2002-731348 [79]; 2002-740172 [80]; 2002-750461 [81]; 2003-066810 [06]; 2003-066893 [06]; 2003-066898 [06]
DNN N2000-028952 DNC C2000-009747
TI New isolated GFR-alpha3 nucleic acid, used to develop products for treating diseases or conditions involving peripheral nervous system or automic nervous system.
DC B04 C03 C06 D16 S03
IN DE SAUVAGE, F J; KLEIN, R D; PHILLIPS, H S; ROSENTHAL, A; ASHKENAZI, A; GODDARD, A; GURNEY, A L; NAPIER, M; WOOD, W I; YUAN, J
PA (GETH) GENENTECH INC
CYC 87
PI WO 9949039 A2 19990930 (200003)* EN 112p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9931944 A 19991018 (200009)
EP 1064376 A2 20010103 (200102) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2002010137 A1 20020124 (200210)
JP 2002507421 W 20020312 (200220) 181p
MX 2000009215 A1 20010501 (200227)
ZA 2000004686 A 20020626 (200251) 137p
NZ 506748 A 20021025 (200274)
ADT WO 9949039 A2 WO 1999-US6098 19990319; AU 9931944 A AU 1999-31944 19990319; EP 1064376 A2 EP 1999-913993 19990319, WO 1999-US6098 19990319; US 2002010137 A1 Provisional US 1997-59263P 19970918, Provisional US 1997-59836P 19970924, Provisional US 1997-63561P 19971028, Provisional US

1997-64248P 19971103, Provisional US 1998-79124P 19980323, Provisional US 1998-81569P 19980413, Provisional US 1998-99803P 19980910, Provisional US 1998-104080P 19981013, Provisional US 1999-123957P 19990312, Provisional US 1999-131445P 19990428, Provisional US 1999-144758P 19990720, Provisional US 1999-145698P 19990726, Cont of US 2000-565278 20000427, US 2001-828366 20010405; JP 2002507421 W WO 1999-US6098 19990319, JP 2000-538000 19990319; MX 2000009215 A1 MX 2000-9215 20000920; ZA 2000004686 A ZA 2000-4686 20000906; NZ 506748 A NZ 1999-506748 19990319, WO 1999-US6098 19990319

FDT AU 9931944 A Based on WO 9949039; EP 1064376 A2 Based on WO 9949039; JP 2002507421 W Based on WO 9949039; NZ 506748 A Based on WO 9949039

PRAI US 1998-81569P 19980413; US 1998-79124P 19980323; WO 1998-US17888 19980828; WO 1998-US18824 19980910; WO 1998-US19330 19980916; WO 1999-US20594 19990908; WO 1999-US21090 19990915; WO 1999-US23089 19991005; WO 1999-US28313 19991130; WO 1999-US28564 19991202; WO 1999-US30999 19991220; WO 2000-US219 20000105; WO 2000-US277 20000106; WO 2000-US4414 20000222; WO 2000-US5841 20000302; WO 2000-US6319 20000310; WO 2000-US6884 20000315; WO 2000-US32678 20001201

AB WO 9949039 A UPAB: 20030124

NOVELTY - Isolated glial-cell-line-derived neurotrophic factor family receptor alpha -3 (GFR alpha 3) polypeptides and polynucleotides are new.

DETAILED DESCRIPTION - A novel isolated (A) nucleic acid (NA) comprises a NA having at least a 65 % sequence identity to:

(a) NA molecule (NAM) encoding a GFR alpha 3 polypeptide comprising the sequence of amino acids 27 to 400 of sequence (XV) shown (400 amino acids in length) or the sequence of amino acids 27 to 369 of sequence (XVII) (369 amino acids in length); or

(b) the complement of an NAM as in (a).

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated NA comprising NA having at least a 65% sequence identity to:

(a) NAM encoding the same mature polypeptide encoded by a cDNA in ATCC No. 209752 (DNA48613-1268) or in ATCC No. 209751; or

(b) the complement of a DNA molecule as in (a);

(2) an isolated NA comprising an NA having at least a 65% sequence identity to:

(a) NAM encoding a GFR alpha 3 polypeptide comprising a sequence of amino acids 84 to 360 of sequence (XV), amino acids 84 to 329 of sequence (XVII), or a sequence of amino acids 110 to 386 of sequence (XX) (888 amino acids in length); or

(b) the complement of an NAM as in (a);

(3) a vector comprising an NA as in (A);

(4) a host cell comprising a vector as in (3);

(5) a polypeptide comprising a sequence having at least 65% sequence identity with amino acid residues 84 to 360 of sequence (XV) or 84 to 329 of sequence (XVII);

(6) a **chimeric** molecule comprising a GFR alpha 3 polypeptide fused to a heterologous amino acid sequence;

(7) an antibody which specifically binds to GFR alpha 3 polypeptide;

(8) measuring agonist binding to a polypeptide comprising an agonist-binding domain of an alpha -subunit receptor, comprising exposing the polypeptide positioned in a cell membrane to a candidate agonist and measuring homo-dimerization or homo-oligomerization of the polypeptide;

(9) measuring autophosphorylation of a polypeptide receptor construct comprising a ligand-binding domain of an alpha -subunit receptor, the intracellular catalytic domain of a tyrosine kinase receptor (TKR), and a flag epitope comprising:

(a) coating a first solid phase with a homogeneous population of eukaryotic cells so that the cells adhere to the first solid phase, where,

positioned in their membranes, the cells have the polypeptide receptor construct;

(b) exposing the adhering cells to an analyte;

(c) solubilizing the adhering cells, thereby releasing cell lysate;

(d) coating a second solid phase with a capture agent which binds specifically to the flag epitope so that the capture agent adheres to the second solid phase;

(e) exposing the adhering capture agent to the cell lysate obtained in (c) so that the receptor construct adheres to the second solid phase;

(f) washing the second solid phase so as to remove unbound cell lysate;

~~(g) exposing the adhering receptor construct to an~~ anti-phosphotyrosine antibody which identifies phosphorylated tyrosine residues in the TKR; and

(h) measuring binding of the anti-phosphotyrosine antibody to the adhering receptor construct;

(10) measuring autophosphorylation of a polypeptide receptor construct comprising a ligand-binding domain of an alpha -subunit receptor, the intracellular catalytic domain of a TKR, and a flag epitope;

(11) a polypeptide comprising an alpha -subunit receptor ligand-binding domain, a flag polypeptide, and an intracellular catalytic domain of a TKR;

(12) a kit comprising a solid phase coated with a capture agent which binds specifically to a flag polypeptide, and a polypeptide comprising an alpha -subunit receptor ligand-binding domain, a flag polypeptide, and an intracellular catalytic domain of a TKR; and

(13) an assay for measuring phosphorylation of polypeptide receptor construct comprising a ligand-binding domain of an alpha -subunit receptor, the intracellular catalytic domain of a kinase receptor, and a flag epitope.

USE - The GFR alpha 3 polypeptides possess neuronal cell activation function typical of the GFR protein family. GFR alpha 3 ligands can be used to stimulate proliferation, growth, survival, differentiation, metabolism or regeneration of GFR alpha 3- and Ret-containing cells. Agents which bind to the GFR alpha 3 molecule could be useful in the treatment of diseases or conditions involving the peripheral nervous system, e.g. such ligands can be used to treat peripheral neuropathies associated with diabetes, human immunodeficiency virus (HIV), or chemotherapeutic agent treatments. Ligands binding to GFR alpha 3 are expected to be useful in the treatment of neuropathic pain, antagonists of GFR alpha 3 are expected to be useful to treat chronic pain of non-neuropathic nature e.g. that which is associated with various inflammatory states. GFR alpha 3 or its agonist or antagonists can be used to treat conditions involving dysfunction of the autonomic nervous system including disturbances in blood pressure or cardiac rhythm, gastrointestinal function, impotence, and urinary continence. Other indications for ligands binding to GFR alpha 3 include post-herpetic neuralgia, shingles, asthma, irritable bowel, inflammatory bowel, cystitis, headache (migraine), arthritis, spinal cord injury, constipation, hypertension, mucositis, dry mouth or eyes, fibromyalgia, chronic back pain, or wound healing. Ligands which act via GFR alpha 3 will be particularly useful to treat disorders of the peripheral nervous system while inducing fewer effects on weight loss, motor function, or on kidney function than would ligands acting via GFR alpha 1 or GFR alpha 2. The products and methods can also be used for qualitatively and quantitatively measuring alpha -subunit receptor activation as well as facilitating identification and characterization of potential agonists and antagonists for a selected alpha -subunit receptor. The products can also be used for detection, diagnosis and production of transgenic animals. Dwg.0/13

TECH UPTX: 20000118
TECHNOLOGY FOCUS - BIOLOGY - Isolation: Using sequences from the neurturin receptor GFRalpha2, a novel, potential member of the GFRalpha family was identified as a mouse expressed sequence tag (EST) in a public gene database (Acc No's W99197, AA041935, and AA050083). A DNA fragment corresponding to this potentially new receptor was obtained by PCR using mouse E15 cDNA as template and PCR primers derived from the mouse EST. The PCR product was then used to screen a lambda gt10 mouse E15 library to obtain a full length clone. A human EST database was searched and an EST (INC3574209) with 61% identity to the murine GFRalpha3 was identified. PCR amplification was then used to screen **cDNA libraries**. A strong PCR product was identified in all libraries analyzed (fetal lung, fetal kidney and placenta). To isolate a cDNA clone encoding this protein, a human fetal lung-pRK5 vector library was selected and enriched for positive cDNA clones by extension of single stranded DNA from plasmid libraries grown in dug- /bung-host using a new a3.R primer. RNA for construction of the **cDNA libraries** was isolated from human fetal lung tissue. Two of the isolated clones were sequenced. These cDNA sequences were designated DNA48613 and DNA48614. Amino acid sequence analysis of DNA48613 (sequence (XV)) revealed a 400 amino acid long open reading frame sequence with a predicted 26 amino acid long N-terminal **signal peptide**. The predicted mature protein is 274 amino acids long, with a calculated molecular weight of 41 kD. Potential N-linked glycosylation sites are similar to those in the mouse sequence. The deduced amino acid sequence of DNA48614 (Sequence (XVII) and comparison to sequence (XV) revealed it to be an alternatively spliced form of DNA 48613, with a 30 amino acid deletion (amino acid positions 127-157, counting from the initiation methionine).

L34 ANSWER 28 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-620189 [53] WPIDS
DNC C1999-180971
TI New avian interleukin-15 that stimulates T lymphocytes, used as adjuvant for avian vaccines.
DC B04 C06 D16
IN CHOI, K; KAMOGAWA, K; LILLEHOJ, H S; TSUSAKI, Y
PA (JAPG) JAPANESE GEON CO LTD; (USDA) US SEC OF AGRIC; (JAPG) NIPPON ZEON KK
CYC 84
PI WO 9951622 A1 19991014 (199953)* EN 65p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
JP 11346786 A 19991221 (200010) 17p
AU 9934720 A 19991025 (200011)
ADT WO 9951622 A1 WO 1999-US7485 19990406; JP 11346786 A JP 1999-98329 19990406; AU 9934720 A AU 1999-34720 19990406
FDT AU 9934720 A Based on WO 9951622
PRAI US 1998-55293 19980406
AB WO 9951622 A UPAB: 19991215
NOVELTY - Avian interleukin-15 (IL-15) polypeptide (I) that stimulates growth of avian T lymphocytes that express gamma delta T cell receptors (TCR) is new.
DETAILED DESCRIPTION - (I) is:
(i) a 143 amino acid (aa) sequence (S1) (given in the specification);
(ii) a fragment of (S1) that stimulates growth of avian T lymphocytes that express gamma delta T cell receptors (TCR), or
(iii) a derivative of (S1) with one or more aa substitutions,

mutations, deletions or insertions, provided they retain at least 70% of the biological activity of (S1) for stimulating the specified lymphocytes and have at least 85% sequence identity with (S1).

INDEPENDENT CLAIMS are also included for the following:

(a) polynucleotides (II) that:

(i) encode (I), or

(ii) hybridize to (i) under stringent conditions;

(b) recombinant vector containing (II);

(c) transformant containing (II);

(d) recombinant **virus** containing (II);

(e) composition for preventing disease in poultry comprising transformants of (c), **virus** of (d) or (I) or its salt;

(f) an adjuvant comprising the same materials as (e); and

(g) method for immunizing birds by administering a cytokine (Ia) that stimulates the immune system and an antigen (Ag) derived from an avian pathogen.

ACTIVITY - Antiviral; antibacterial; antiprotozoal; anticoccidiosis.

MECHANISM OF ACTION - (I) is a growth factor for T cells that express the gamma delta T cell receptor, so stimulates the immune response to a co-administered antigen. When lymphocytes from chicken spleen were stimulated with concanavalin A (ConA), then grown in presence of avian IL-15, they showed high proliferative capacity (stimulation index about 2.5-2.8), higher than that achieved with ConA alone. After 29 days culture, most cells were positive for the gamma delta TCR and these cells had high spontaneous cytolytic activity against the chicken lymphoblastoid tumor cell line LSCC-RP9 at effector:target ratios 2-16:1.

USE - (I), or transformed cells or recombinant **viruses** that express it, are used as adjuvant for vaccines used in poultry, specifically chickens, to protect against a wide variety of diseases, e.g. those caused by **viruses**, Eimeria or other protozoa, or Mycoplasma gallisepticum.

ADVANTAGE - Administration of (I) improves the immune response to vaccinating antigens. Compositions containing recombinant cells or **viruses** can be stored, optionally in lyophilized form, under normal conditions, obviating the need for storage in liquid nitrogen.

Dwg.0/10

TECH UPTX: 19991215

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Protein: (I) is especially (S1) and is expressed in chickens, particularly in skeletal muscle, caecal tonsil, small intestine, heart, liver, oviduct and/or spleen. The first 20 aa of (S1) represents a **signal peptide**.

Preferred Composition: Compositions of (e) also contain an Ag, particularly where expressed from a recombinant **virus** (which may be the same as the vector expressing IL-15, or a separate vector). Specified Ag are : HN or F of Newcastle disease **virus**; gB, gC or UL32 of infectious laryngo-tracheitis **virus**; gB, gC, gH, gL, gI or gE of Marek disease **virus**; surface antigens of protozoa, particularly Eimeria; VP2 of infectious bursal disease **virus**, or the 40 kD polypeptide of Mycoplasma gallisepticum.

Preferred Method: In method (g), (Ia) is especially (I) and Ag is present in viral vectors, **viruses** or transformants.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid is a 800 bp sequence (S2) (given in the specification), its fragments or a molecule that hybridizes with it.

Preparation: A **cDNA** expression **library** was prepared from the CD4+ chicken T cell hybridoma P34 and screened using a rabbit antibody raised against a protein fraction from P34-conditioned medium that had a growth promoting effect on T cells. Inserts in positive phages were recloned into plasmids and one recombinant plasmid (pUC-chIL-15) was

sequenced; it included the sequence (S2). Once isolated the cDNA (or its fragments or variants prepared by usual methods) can be expressed in usual vector/host systems, optionally in the form of a **fusion** protein, or used to make recombinant **viruses** conventionally.

L34 ANSWER 29 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-326923 [27] WPIDS
CR 2002-009367 [72]
DNC C1999-096693
TI **Fusion** protein of signal sequence and calpastatin.
DC B04
IN POTTER, D A; SKOLNIK, P R
PA (NEWE-N) NEW ENGLAND MEDICAL CENT HOSPITALS INC
CYC 22
PI WO 9922756 A1 19990514 (199927)* EN 55p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9913814 A 19990524 (199940)
US 6015787 A 20000118 (200011)
ADT WO 9922756 A1 WO 1998-US23526 19981104; AU 9913814 A AU 1999-13814 19981104; US 6015787 A US 1997-964302 19971104
FDT AU 9913814 A Based on WO 9922756
PRAI US 1997-964302 19971104
AB WO 9922756 A UPAB: 20020105
NOVELTY - A **fusion** protein (I) comprises (a) a signal sequence (II) able to deliver (I) to a eukaryotic cell and (b) a calpastatin peptide (III) or its variants.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for inhibition of calpain in a cell by treatment with (I).

ACTIVITY - Antiviral; anti-aggregation; anti-inflammatory; immunosuppressant; antithrombotic; antineurodegenerative; cardiovascular. Purified platelets were incubated for 30 min at 37 deg. C with 45 mu M of the **fusion** protein, calpastat, of formula AAVALLPAVLLALLAPEKLGERDDTIPPEYRELLEKKTGV then aggregation induced with 0.1-1 unit/ml thrombin. This treatment inhibited aggregation but a variant of calpastat without the **signal peptide** was inactive.

MECHANISM OF ACTION - (I) inhibit the calcium-activated cytosolic **proteases** mu - and/or m-calpain that are involved in (pathological) cytoskeletal remodeling, cellular adhesion, shape change and motility (e.g. of invasive cancer cells). A reaction buffer (pH 7.5) was combined with 0. 2 mM of succinyl-LLVY-AMC (7-amino-4-methylcoumarin), 5 mM calcium chloride and various amounts of calpastat. At time zero, 4 mu g pure mu -calpain were added (final concentration 70 nM), and the rate of release of AMC was measured fluorimetrically (excitation 360 nm; emission 466 nm). Calpastatin inhibited cleavage of the substrate with IC50 50 nM.

USE - (I) are specifically used:

(a) to prevent aggregation and degranulation of platelets (e.g. during storage);

(b) to inhibit hypoxia-induced sickling of erythrocytes (during storage, facilitating subsequent transfusion of autologous cells for treatment of sickle cell crises); and

(c) to inhibit activation of human immune deficiency **virus** provirus in infected cells (or similarly for other **viruses** regulated by NF-kappaB).

Other disclosed uses are: to treat or prevent inflammation (e.g. arthritis or asthma), unwanted immune responses (e.g. transplant rejection), restenosis (associated with angioplasty), cancer, subarachnoid hemorrhage, vasospasm, muscular dystrophy, cataracts and traumatic birth injury; to prevent spread of platelets on surfaces (e.g. when applied to the surface of stents, catheters etc.); to reduce coronary thrombosis in

by-pass surgery and angioplasty; to treat myocardial infarction, or to prevent progression of infarction (myocardial or cerebral).

ADVANTAGE - (I) has a reversible inhibitory effect and enters cells easily. It allows platelets to be stored cold with reduced change in shape.

Dwg.0/16

TECH UPTX: 19990714

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred peptides: (III) have formula X1X2LGX5X6X7X8TIPPX13YX15X16LLX19

X1 and X13 = E, D or K;
X2 = K, E, A or N;
X5 = E, K or I;
X6 = R, K or D;
X7 = E or D;
X8 = D, V, S, G or E;
X15 = R, K or Q;
X16 = E, H, L or K;
X19 = E, D, N, A or V

. Particularly preferred is sequence (4) EKLGERDDTIPPEYRELLEKKTGV (4). (II), particularly C-terminal with respect to (III), is derived from Kaposi fibroblast growth factor and has formula (3) AAVALLPAVLLALLAP (3).

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) are made by standard methods of recombinant DNA manipulation. The specification includes two suitable nucleic acid sequences.

L34 ANSWER 30 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-277254 [23] WPIDS
DNC C1999-081433
TI Polypeptides identified by the **signal** sequence **trap** method from a human cDNA library.
DC B04 D16
IN FUKUSHIMA, D; SHIBAYAMA, S; TADA, H
PA (ONOY) ONO PHARM CO LTD; (FUKU-I) FUKUSHIMA D; (SHIB-I) SHIBAYAMA S; (TADA-I) TADA H
CYC 22
PI WO 9918126 A1 19990415 (199923)* JA 291p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP KR US
EP 1022286 A1 20000726 (200037) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
KR 2001015711 A 20010226 (200156)
US 2002102542 A1 20020801 (200253)
ADT WO 9918126 A1 WO 1998-JP4514 19981006; EP 1022286 A1 EP 1998-945638 19981006, WO 1998-JP4514 19981006; KR 2001015711 A KR 2000-703767 20000407; US 2002102542 A1 WO 1998-JP4514 19981006, US 2000-529063 20000407
FDT EP 1022286 A1 Based on WO 9918126
PRAI JP 1997-274674 19971007
AB WO 9918126 A UPAB: 19990616
NOVELTY - Polypeptides are new identified from a human placental cDNA library by the **signal** sequence **trap** (SST) method.

DETAILED DESCRIPTION - Twenty-seven new polypeptides are identified from a human placental cDNA library by the SST method. The sequences of these polypeptides are given.

INDEPENDENT CLAIMS are included for:

(1) DNA sequences encoding all or part of the popypeptides and for DNA hybridising with these;

(2) vectors encoding the DNA;

(3) host cells transformed by the vectors;

(4) the preparation of the polypeptides by culture of the transformants;

(5) monoclonal or polyclonal antibodies recognising the polypeptides or their fragments.

ACTIVITY - The polypeptides have a broad range of physiological activity, including immunisation against and inhibition of infections, allergies and cancer; regulation of tissue formation and repair; activin/inhibin activity; chemokine/cytokine activity; blood coagulation regulation; and receptor/ligand agonist or antagonist activity.

USE - Prevention and treatment of disorders including infections by bacteria, yeasts and **viruses** (including HIV) and protozoa; metabolic and hormonal disorders; immune disorders (including severe combined immunodeficiency (SCID) and AIDS; thrombosis; cancer; and traumatic or surgical wounds.

Dwg.0/1

L34 ANSWER 31 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-264042 [22] WPIDS
DNC C1999-077944
TI **Signal-peptide** containing proteins that modulate cellular processes.
DC B04 D16
IN GEARING, D P; MCCARTHY, S A; PAN, Y
PA (MILL-N) MILLENNIUM BIOTHERAPEUTICS INC; (MILL-N) MILLENNIUM PHARM INC
CYC 22
PI WO 9918243 A1 19990415 (199922)* EN 123p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9897907 A 19990427 (199936)
EP 1029034 A1 20000823 (200041) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9918243 A1 WO 1998-US21151 19981006; AU 9897907 A AU 1998-97907 19981006; EP 1029034 A1 EP 1998-952139 19981006, WO 1998-US21151 19981006
FDT AU 9897907 A Based on WO 9918243; EP 1029034 A1 Based on WO 9918243
PRAI US 1998-14347 19980127; US 1997-61143P 19971006; US 1997-61149P 19971006; US 1997-61159P 19971006; US 1998-4206 19980108; US 1998-10674 19980122
AB WO 9918243 A UPAB: 19990609
NOVELTY - Nucleic acids (I) encoding the **signal-peptide** -containing molecules leucocyte-specific protein-1 (LSP-1), proliferin analog I (PA-I) and thrombopoietin analog protein 1 (TAP-1).

DETAILED DESCRIPTION - DETAILED DISCLOSURE - (I):

(i) is any of sequences 1 (2462 bp, for human LSP-1), 3 (678 bp, the coding region of 1), 4 (933 bp, for murine PA-I), 6 (762 bp, the coding region of 4), 7 (532 bp, for human TAP-1) or 9 (258 bp, the coding region of 7);

(ii) encodes sequences 2 (226 amino acids (aa), human LSP-1), 5 (253 aa, murine PA-I) or 8 (86 aa, human TAP-1);

(iii) is present in the plasmid of ATCC 98554;

(iv) encodes a natural allelic variant of 2, 5 or 8;

(v) is at least 60% homologous with, or comprises a fragment of at least 601 bp of, (i);

(vi) encodes a polypeptide at least 60% homologous with (ii);

(vii) encodes a fragment of (ii) containing at least 15 contiguous aa;

(viii) is complementary to, or hybridizes under stringent conditions with, any of (i)-(vii), or

(ix) comprises any of (i)-(vii) plus a sequence encoding a heterologous peptide.

INDEPENDENT CLAIMS are also included for the following:

(a) vectors containing (I);
(b) host cells transfected with this vector;
(c) recombinant production of polypeptides (II) by culturing these cells;
(d) (II) which are:
(i) at least 60% homologous with 2, 5 or 8,
(ii) encoded by sequences at least 60% homologous with 1, 3, 4, 6, 7 or 9,
(iii) are natural allelic variants of 2, 5 or 8, or
(iv) are fragments of 2, 5 or 8 containing at least 15 contiguous aa;
(e) antibodies that bind selectively to (II), and
(f) modulation of (II) activity by treating it, or cells expressing it, with a binding agent.

ACTIVITY - Antiangiogenic; anticancer; anti-inflammatory; anti-arthritic; anti-thrombocytopenic.

MECHANISM OF ACTION - (I) and its modulators are involved in signal transduction; inflammatory responses; growth, proliferation, differentiation and survival of cells; angiogenesis; maturation of hematopoietic stem cells and erythroid precursors; megakaryocytopoiesis and thrombopoiesis.

USE - Antibodies, or other binding agents, specific for polypeptides (II) encoded by (I), are used to detect (II), for diagnosis, prognosis and monitoring of treatment of (II)-related diseases, also for purification of (II). Probes and primers based on (I) can be used to detect (I), particularly mRNA, by hybridization, including detection of genetic alterations.

(II) may also be used to identify agents (A) that bind to and/or modulate activity of (II). Other uses of (I) are in chromosome mapping, identification of individuals (tissue typing) and in forensic studies. LSP-1, PA-I and TAP-1 proteins and nucleic acids are modulators of cellular processes, particularly they (and (A)) are used to treat or prevent diseases associated with deregulation of angiogenesis, immune responses and hematopoiesis, e.g. cancer, arthritis (and other inflammatory diseases), thrombocytopenia (caused by cancer treatment, bone marrow transplant, human immune deficiency **virus** infection etc.), intravascular coagulation, iron deficiency etc.

Dwg.0/10

TECH UPTX: 19990609

TECHNOLOGY FOCUS - BIOLOGY - Preferred assay: Modulators of (II) are identified from (a) direct detection of test compound/(II) binding; (b) in a competitive binding assay, or (c) by measuring activity of (II). Modulators are e.g. antibodies, antisense nucleic acids or ribozymes. Preparation: Antibodies are made by usual methods of immunization and cell **fusion**.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: A human bone marrow **cDNA library** was prepared in the vector ptrAP1 (for expression of **fusions** with alkaline phosphatase, AP), used to transform human embryonic kidney fibroblasts and transfectants selected for AP expression. One positive clone, LSP-1, included a partial open reading frame and this was used to search a database of expressed sequence tags (EST). Three positive ESTs were identified in the IMAGE database and these were assembled to produce the complete sequence. The gene for LSP-1 has been mapped to chromosome 7q21-q22. The PA-I sequence was isolated similarly in EST databases, using the human growth hormone as probe. A partial TAP-1 cDNA was identified in an EST database, using the murine thrombopoietin sequence as probe, and this used to identify a partial human clone (deposited in ATCC 98554), and this in turn used to identify other TAP-1 cones conventionally. Once isolated, these cDNA, optionally after modification, can be expressed in usual vector/host systems,

optionally as **fusion** proteins.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Fragments of (I) and (II) may be produced by standard chemical synthesis.

L34 ANSWER 32 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 1996-268615 [27] WPIDS
DNC C1996-085428
TI Molecular chimaera for use in enzyme gene therapy - is activated in a target cell to express a secretable enzyme which cleaves a prodrug outside the cell into a cytotoxic or cytostatic agent.
DC B04 D16
IN DEV, I K; MOORE, J T; OHMSTEDE, C
PA (WELL) WELLCOME FOUND LTD
CYC 69
PI WO 9616179 A1 19960530 (199627)* EN 73p
RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN
AU 9538773 A 19960617 (199638)
ZA 9509846 A 19970730 (199735) 70p
EP 792366 A1 19970903 (199740) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
AU 695375 B 19980813 (199844)
JP 10509326 W 19980914 (199847) 70p
ADT WO 9616179 A1 WO 1995-GB2716 19951120; AU 9538773 A AU 1995-38773 19951120; ZA 9509846 A ZA 1995-9846 19951120; EP 792366 A1 EP 1995-937956 19951120, WO 1995-GB2716 19951120; AU 695375 B AU 1995-38773 19951120; JP 10509326 W WO 1995-GB2716 19951120, JP 1996-516671 19951120
FDT AU 9538773 A Based on WO 9616179; EP 792366 A1 Based on WO 9616179; AU 695375 B Previous Publ. AU 9538773, Based on WO 9616179; JP 10509326 W Based on WO 9616179
PRAI GB 1994-23367 19941118
AB WO 9616179 A UPAB: 19960710
A molecular **chimera** for use with a prodrug comprises a transcriptional regulatory **DNA** sequence (I) activated in a targeted mammalian cell and a **DNA** sequence (II) operably linked to (I) encoding a secretion **signal peptide** and a heterologous enzyme, so that on expression of (II) the enzyme passes through the plasma membrane and catalyses extracellular conversion of the prodrug into a cytotoxic or cytostatic agent.

USE - The **chimera** is used in a claimed medicament to exert a therapeutic effect preferentially in cells with a pathological disorder, e.g. cancer (partic. hepatocellular carcinoma, non-seminamatous carcinoma of the testis, and certain teratocarcinoma's and gastrointestinal tumours).

ADVANTAGE - Cleavage by a pathology associated **protease** provides a mechanism of elevating the fidelity of targeted enzyme prodrug therapy. The vector is partic. a retroviral shuttle vector, which has a high efficiency of gene delivery to the targeted tissue, sequence-specific integration regarding the **viral genome** and little rearrangement of delivered **DNA** compared to other **DNA** delivery systems.

Dwg.0/6

L34 ANSWER 33 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 1992-415766 [50] WPIDS
CR 1998-076485 [07]; 1998-311405 [27]; 1998-321520 [28]

DNC C1992-184551
TI Diagnosis of stealth **virus**-associated disease - using a permissive cell line, useful in patients with chronic fatigue syndrome.
DC B04 C06 D16
IN MARTIN, W J
PA (MART-I) MARTIN W J
CYC 34
PI WO 9220787 A1 19921126 (199250)* EN 121p
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU BG BR CA FI HU JP KP KR LK MG MW NO PL RO RU SD US
AU 9220112 A 19921230 (199313)
EP 585390 A1 19940309 (199410) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
AU 666483 B 19960215 (199614)
EP 585390 A4 19950531 (199615)
NZ 242876 A 19970822 (199741)
ADT WO 9220787 A1 WO 1992-US4314 19920522; AU 9220112 A AU 1992-20112 19920522, WO 1992-US4314 19920522; EP 585390 A1 EP 1992-913204 19920522, WO 1992-US4314 19920522; AU 666483 B AU 1992-20112 19920522; EP 585390 A4 EP 1992-913204 ; NZ 242876 A NZ 1992-242876 19920522
FDT AU 9220112 A Based on WO 9220787; EP 585390 A1 Based on WO 9220787; AU 666483 B Previous Publ. AU 9220112, Based on WO 9220787
PRAI US 1991-763039 19910920; US 1991-704814 19910523
AB WO 9220787 A UPAB: 19980715
Diseases associated with stealth **virus** (SV) are diagnosed in human or animals by detecting SV in a body sample.

Also new are (I) in vitro culture of SV by inoculating it into a permissive cell line; (2) isolated SV; (3) SV-infected MRC-5 cells; (4) purified SV-associated toxin (I); (5) kits for culture and detection of SV; (6) purified antibodies against SV; (7) nucleic acid probes which hybridise specifically with SV nucleic acid; (8) SV nucleic acid; (9) vaccines contg. SV antigens (or their fragments) or vectors able to produce such antigens.

SV is detected (1) by inoculating a permissive cell line and examining for cytopathic effects (CPE); (2) by isolating viral DNA and testing for specific hybridisation. (3) by reactivity with specific antibody or (4) by detecting presence of (I).

USE/ADVANTAGE - Used to diagnose chronic fatigue syndrome (CFS, or related conditions in animals), atypical neurological, psychiatric, rheumatological or autoimmune-like diseases; or atypical diseases of liver, testis, ovary, etc.. It can also be used to detect SV contamination in foods or other products. SV infections can be treated with e.g. (I), ciguatera toxin, alpha-interferon, Li or **cerulenin**, while SV infections can be monitored by determining levels of SV and/or its toxin. The vaccines are used to protect against SV infection
Dwg.0/17

L34 ANSWER 34 OF 35 WPIDS (C) 2003 THOMSON DERWENT
AN 1988-133691 [20] WPIDS
DNC C1988-059820
TI Antibiotic and enzyme inhibitor **cerulenin** microbiological prodn. - by fermentation of microorganism IP45 under aerobic conditions in the presence of a zeolite molecular sieve.
DC B04 C03 D16
IN FLECK, W; IHN, W; SCHLEGEL, B; STENGEL, C; TRESSELT, D K
PA (DEAK) AKAD WISSENSCHAFTEN DDR
CYC 1
PI DD 252616 A 19871223 (198820)* 5p
DD 252616 B 19900620 (199046)
ADT DD 252616 A DD 1986-294232 19860908

PRAI DD 1986-294232 19860908
AB DD 252616 A UPAB: 19930923
The microorganism IP45 (belonging to the fungi imperfecti) is subjected to fermentation under aerobic and sterile conditions at 25-37 deg.C in a liquid nutrient medium contg. carbon- and nitrogen-sources, mineral salts and ''Zeosorb'' (RTM) molecules sieve for 2-4 days; (b) the resulting **cerulenin** is isolated from the culture filtrate by extraction with an organic solvent at pH 5.0-6.6; and (c) the prod. is purified by subsequent concentration, chromatographic purificn. and recrystallisation.

USE/ADVANTAGE - **Cerulenin** has antibiotic activity against fungi, yeasts and gram-positive bacteria. As an inhibitor of fatty acid synthetase and polyketide synthetase, **cerulenin** can also be used in the hybrid biosynthesis of new hybrid antibiotics of potential use in the chemotherapy of disease due to tumours, **viruses** and microorganisms. **Cerulenin** is the exclusive fermentation product, being produced in good yields uncontaminated by steroidal antibiotics.
0/0